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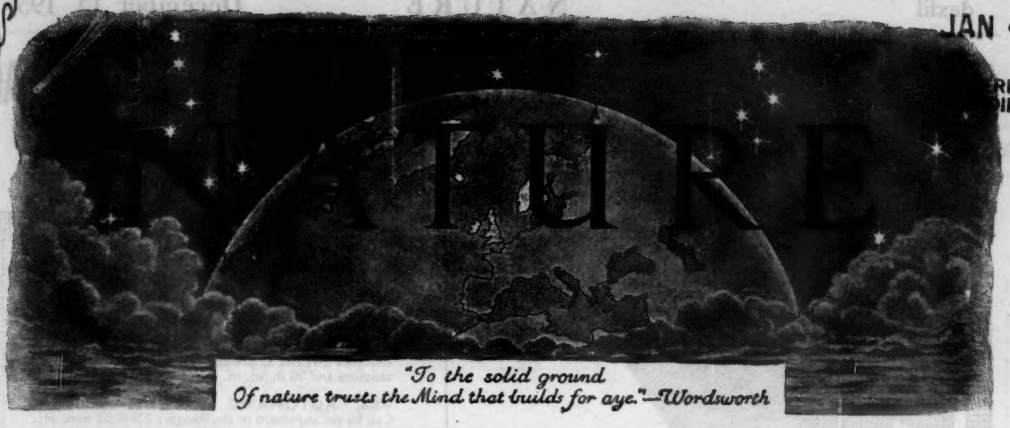

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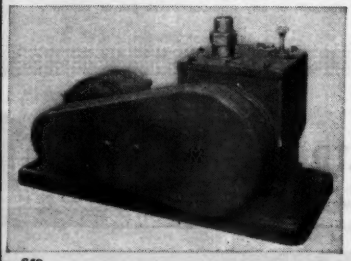

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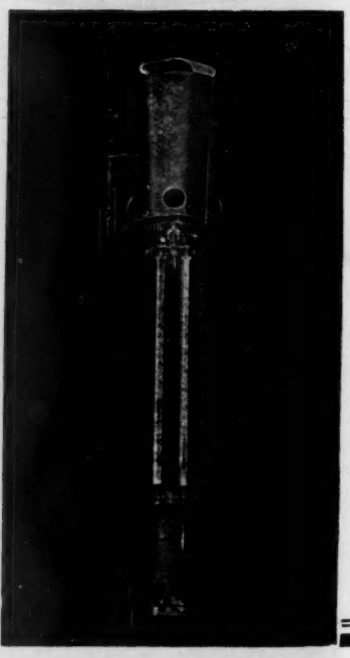

NATURE

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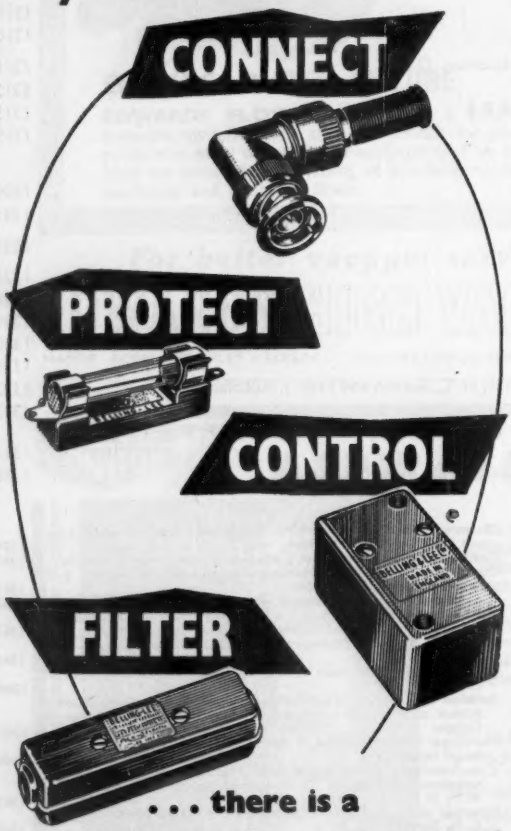

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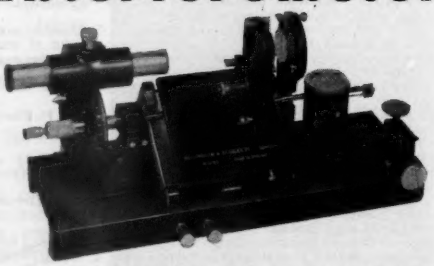

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ANGLO-AMERICAN RELATIONS IN THE NUCLEAR AGE

MORE than five years ago, Dr. J. B. Conant, in the Stevenson Lecture for 1952, discussed frankly the broad question of Anglo-American co-operation in the modern world. The successful launching by the U.S.S.R. of two Earth satellites is only one of a series of developments that has since convinced the United States as well as Britain that the security of the free world is not to be found in the achievements of individual countries, but rather in a more effective co-operation which avoids duplication of effort and waste of precious resources of trained man-power and materials. The case of J. R. Oppenheimer three years ago brought to the front a new conception of national security, and raised questions regarding the co-operation of scientists with government and the organization of security to which clear answers are still being sought. Later that year, indeed, in one of his Reith Lectures, Sir Oliver Franks discussed some of these problems. The Supreme Court's judgment in three cases on civil liberties last June dealt a blow to McCarthyism which should at least facilitate closer Anglo-American co-operation and understanding, just as in Britain the Government statement on January 29 and the earlier statement of March 1956 on the findings of the Conference of Privy Councillors on Security should help to establish confidence in both countries in the effectiveness of the British security system, and in the care taken to reconcile the needs of public security and the claims of the individual.

Moreover, there has been during these years an able exposition in the United States of the dynamic conception of security by such men as H. S. Commager, R. M. MacIver, R. M. Hutchins and others, and the Geneva Conference on the Peaceful Uses of Nuclear Energy resulted in a marked advance in the release of information in a field where secrecy has hitherto hampered scientific advance as well as technical development. The opening of the world's first nuclear power station at Calder Hall in October 1956 showed that in technological development, as well as at the frontiers of science, Britain has much to contribute. Even in the field of defence, there has been a substantial exchange of information between Britain and the United States in such fields as guided missiles. In July 1954, Mr. Duncan Sandys, then Minister of Supply, assured Parliament that the arrangements made for co-operation should enable both countries to make the most productive use of their available scientific and technical resources in this field and help to accelerate the development and introduction of the missiles urgently needed for common defence. After visiting Washington early this year, now as Minister of Defence, he told Parliament on February 6 that, after reviewing the arrangements previously made for collaboration in military research and development, with particular reference to guided rockets, it had been decided to extend still further the common work.

It is against this background that the statement which the Prime Minister made in Parliament on October 29 regarding his visit to the United States and Canada with the Foreign Secretary, and the Declaration of Common Purpose issued by Mr. Macmillan and the President of the United States at the end of their talks in Washington, must be considered. The main purpose of the Declaration was to establish the principle of interdependence of the countries of the free world, and the Declaration affirms that only in genuine partnership, by combining their resources and sharing tasks in many fields, can progress and safety be found. "For our part, we have agreed that our two countries will henceforth act in accordance with this principle."

The Declaration affirms that the two countries regard their possession of nuclear-weapon power as a trust for the defence of the free world, and that they plan to discuss their ideas as to collective security with all their partners and to reinforce such efforts by co-operative economic effort. The plans for developing a European Free Trade Area in association with the European Common Market are welcomed. It is also recognized that, especially in the less-developed countries, there should be a steady and significant increase in standards of living and economic development.

In his statement in the House of Commons, Mr. Macmillan said that the two Governments would seek to secure the participation of all their allies, and the support of other free nations, in a common partnership. The Canadian Government had expressed itself as ready to subscribe to the principle of interdependence and to join in the common effort to make it effective. Neither the Prime Minister, even when specifically questioned by the leader of the Opposition, nor the Declaration, as circulated in *Hansard*, referred to the announcement in Washington on October 24 that two study groups had already been set up by the President and the Prime Minister. To the Strauss–Plowden Group was assigned the responsibilities of making recommendations in the field of nuclear relationship and co-operation. The Powell–Quarles group was asked to make recommendations in the field of military defence, particularly those problems dealing with missiles and rockets.

Replying to Mr. Gaitskell, who, with reason, seized on the exchange of scientific information and the provision of much closer collaboration as the most valuable feature of these talks, Mr. Macmillan pointed out that full interchange of information between Britain and the United States already existed on the peaceful uses of nuclear energy, but he hoped that the Declaration would extend such co-operation and bring all our friends and allies, especially in the North Atlantic Treaty Organization, into full partnership. Whether a complete exchange of scientific information in the latter Organization is to become possible

depends on the willingness of Congress to meet the President's wishes.

The Joint Parliamentary Under-Secretary of State for Foreign Affairs, Lord Gosforth, replying for the Government in the debate on the Queen's Speech in the House of Lords on November 7, could give no detailed information about the exchanges in progress. He realized the difficulties inherent in the Atomic Energy Act, 1954, but Britain has been assured that the Declaration is one of substance. Lord Stansgate, who asked the question, had pointed out that the Atomic Energy Act, 1954, was a very lively party political issue in the United States, and it was by no means certain that the President would receive the support he desired.

The debate in the House of Commons added little to the Declaration and the Prime Minister's accompanying remarks. Speaking on November 5, Mr. Macmillan commented that the American people are no longer confident that even their great country could do everything itself without allies to secure its own survival, still less the survival of the ideals for which they stood. The days of national self-sufficiency have gone, and we have in the Declaration the first common agreement that the free world can no longer afford to waste its resources in skill and money, but must make its joint effort truly co-operative.

The implications of the Declaration have still to be worked out, as the Prime Minister in fact recognized, and they were to some extent indicated by Mr. Duncan Sandys on November 7. Mr. Sandys pointed out that, although there has already been a good deal of collaboration between the two countries, it has been limited largely to the exchange of information and has not prevented wasteful duplication of effort, both in research and production. Moreover, we have reached the point where in practice the Atomic Energy Act, 1954, tends to frustrate agreements to collaborate in almost any field, because practically every modern weapon of importance now carries a nuclear warhead. Even unrestricted exchange of information is not enough. To make full use of our resources of brain, skill, experience and experimental facilities, we must go so far as practicable in planning and executing a common, rationalized programme of research and development, within which each country must undertake tasks and responsibilities in accordance with its capacity, and each must assist the other to the utmost in carrying them through.

Before considering what is involved in the formulation, let alone the execution, of such a programme, even in its scientific and technical aspects, it is as well to recall the fundamentals which Dr. Conant and Sir Oliver Franks stressed. Although McCarthyism has lost some of its force, secrecy is still an important issue, and the modification of the Atomic Energy Act, 1954, may well depend on whether the U.S. Senate is satisfied that the American secrets will be safe with her partners. Now, as Dr. Conant observed, if we are to help the United States in this matter, especially towards the adoption of that positive conception of security which her own leaders have formulated so ably, we must try to understand conditions in the United States, and counsel rather than scold. Co-operation will be the smoother the more scientists, academic men and government officials are able to operate in a framework which is similar in both countries. Furthermore, the conditions most favourable to creative work and scientific advance do not vary as national frontiers are crossed.

Sir Oliver Franks, in his Reith Lectures, gave much the same counsel, pointing out further that, even on major issues, there would have to be give and take between the partners, that Britain must be more articulate about her policies, and also be careful to demonstrate her ability to perform. We cannot be content to rest on the Calder Hall achievement since those lectures were delivered, and it is as well to examine more closely some of the consequences for our whole economy, as well as for our scientific and technological effort, if the hopes of the Declaration are to be realized.

First, it should be noted that this matter affects the whole of Britain's scientific and technical man-power ; it concerns the universities and technical colleges as well as Government establishments and industry. Mr. Chuter Ede sought to make a party political point, but he and Mr. Callaghan were quite right to remind the House of Commons that the question of Anglo-American co-operation in science and in defence is inseparably related to education. Resources of scientific and technical man-power are determined, both qualitatively and quantitatively, by the character of the educational system and the manner in which it is geared to a country's needs and traditions.

This needs to be remembered in considering how far the structure of the scientific and technological institutions and the organization of research in Britain are appropriate to the needs of to-day. What needs particularly to be stressed at this juncture is that educational systems are not usually exportable ; differences in organization and emphasis are inevitable between those of Great Britain and the United States, if each is to give the best service to its own community. But there is no virtue in difference for difference's sake, and care might well be taken to make the British outlook and ideals readily understandable in the United States. How important this can be is readily seen in the storm that arose earlier this year over security checks in so far as they involved university teachers. In discussing the personal inquiries which have been made of university tutors, among others, regarding candidates for Government posts involving access to classified material bearing on the security of the State, the Council of the Association of University Teachers scarcely gave sufficient weight to the very real security problem.

Such an unrealistic attitude is unhelpful and at the present time could easily hinder the establishment of that confidence in the security practices and policy of Britain which is an essential preliminary to the modification of the Atomic Energy Act, 1954. The point is one which is not easily over-stressed, and scientists and technologists as well as other professional men

should take particular care to see that security issues are not raised or discussed in a manner calculated to raise doubts as to British good faith or efficiency in so vital a matter. Further, by the consistent exposition of the positive conception of security to which the National Science Foundation gave admirable expression in its last annual report, they could contribute also to the formation of a climate of opinion calculated both to encourage the smooth operation of the unofficial checks and balances which are usually more effective than official action, and the vision, sense and vigilance which are the ultimate safeguard. It might well be worth while exploring Dr. Conant's suggestion of a Joint Anglo-American Commission to examine the security issue, if indeed that could not be better done by the academic alliance he also suggested.

ANNUAL REVIEW OF BIOCHEMISTRY—A PERENNIAL PROBLEM

Annual Review of Biochemistry

Edited by J. Murray Luck, in association with Frank W. Allen and Gordon Mackinney. Pp. x+768. (Palo Alto, Calif.: Annual Reviews, Inc., 1957.) 7 dollars.

THE twenty-sixth volume of the "Annual Review of Biochemistry" shows several changes. The number of chapters is reduced from twenty-three to twenty, the sections on lipid chemistry, cancer, immunochemistry, viruses, cellular particles, drugs and fungi being omitted and replaced by sections on X-ray studies of compounds of biological interest, biochemistry in the U.S.S.R., biochemistry of muscle, and clinical applications of biochemistry. In part, these changes reflect the established practice of not reviewing annually certain aspects of biochemistry. However, in this issue, the editors have announced their intention of transferring to sister volumes topics which seem more appropriate to microbiology or to plant or animal physiology. It is to be hoped that this does not mean that certain topics of interest to biochemists are to be permanently removed from this book. One pleasing feature of the "Annual Review of Biochemistry" is that it is a book for biochemists to browse in, in addition to providing an annual refresher course; it is to be hoped that this feature can be retained.

In so far as individual chapters are concerned, the editors claim to insist that reviews shall be critical appraisals and not summaries. Nevertheless, it is clear from reading this book that the style of the individual chapter is more often dictated by the state of the subject than by editorial policy. Thus, Steinberg and Mihalyi in their chapter on the chemistry of proteins have, in the space of thirty-four pages, welded together 340 references into an unusually lucid, critical and well-balanced review. The chapter is, in a sense, a tribute to those who have contributed to methods of determining protein structure, since a new approach to the vexed problem of protein purity, by considering proteins of known chemical structure, is now possible, and sections on genetic determination of protein structure, and relation of structure to function have an atmosphere of reality not previously possible. Dorfman, on the other hand, in a chapter on the biochemistry of steroid hormones has been content, for the most part, to list the many steroids formed by animals and their tissues without indicating how they are formed. Indeed, one gets the impression from this chapter that with steroids the end rather than the means to the end is the important consideration, and a thorough briefing in steroid biochemistry would appear to be an essential prerequisite in attempting to read this section.

Many authors have complained in their prefatory remarks of the vast extent of literature to be reviewed. One effect of this seems to be that critical considerations have to be so brief that they perhaps lose their value. This type of difficulty was evident in the section on carbohydrate metabolism by de Duve and Hers. This would perhaps suggest that the summary may, after all, be the best way of dealing with much of the new knowledge in those topics reviewed annually. In cases where a notable change in the subject has occurred during the year, more space could then be devoted to a comprehensive and critical account. In this connexion, in the present volume, the revision of ΔF° for hydrolysis of the pyrophosphate bond in adenosine triphosphate from 12 down to 7 kcal./mole is considered only briefly by Mahler and by Weber. One would have thought that a re-evaluation of this magnitude of one of the most important thermodynamic considerations in biochemistry would have received more than passing mention. It would be interesting to know, for example, why previous estimates have been so much in error, and how thermodynamic balance sheets such as that for the triosephosphate dehydrogenase reaction have passed the auditors in the past.

In the case of those topics which do not merit annual review, the present policy of publishing a critical type of review from time to time would seem to be admirable. In this volume, the chapters by Kendrew and Perutz on X-ray studies of compounds of biological interest and by Rimington on hæm pigments and porphyrins are excellent illustrations of what can be achieved in this connexion.

The chapter by Jakob A. Stekol on biochemistry in the U.S.S.R. seems to raise a further problem in relation to future policy. An attempt is made here to review the whole of research in animal biochemistry by Soviet biochemists in recent years. The author must be congratulated for attempting this impossible task. It was difficult not to conclude after reading this chapter that many of the papers must have suffered in translation, for several of the abstracted comments are scarcely intelligible. This was particularly true of the somewhat ideological discussion on the last page. It is to be hoped that in future volumes of the "Annual Review of Biochemistry" it will be unnecessary to review Russian biochemistry in a separate chapter, but that it will be possible to record the contributions of Soviet biochemists in the ordinary chapters of this book.

The prefatory chapter this year is by Sir Rudolph Peters and is entitled "Forty-five Years of Biochemistry". Written in a most persuasive and charming manner, it not only records Sir Rudolph Peters's recollections of personalities and landmarks in the history of the subject, but also his conclusions as to the future of the subject and the training of biochemists. The editors are to be especially congratulated on their choice of author for this particular chapter this year. PHILIP J. RANDLE

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(London and New York: Pergamon Press, Ltd., 1955 and 1956.)

THE two volumes entitled "Vistas in Astronomy" are dedicated to F. J. M. Stratton, professor emeritus of astrophysics in the University of Cambridge, "by his friends and admirers everywhere". The idea of this tribute originated with Dr. Arthur Beer, and he wrote in 1952 to a number of astronomers and geophysicists. He received in reply 192 contributions by 215 authors belonging to twenty-six different countries; the printed text occupies 1,732 pages. As its editor had hoped, the work surpasses the ordinary dimensions of a *Festschrift*: it constitutes "a generous and thorough cross-section through the whole of contemporary astronomy and the allied sciences". It imposed an enormous task upon Dr. Beer, but he has been recompensed by a well-merited success.

None is more worthy of this universal tribute than Prof. Stratton, who is one of the best-known figures of contemporary astronomy. His scientific career opened in 1906 with the publication of a paper "On Planetary Inversion". This paper was followed by many others, some of which have become the bedside companions of numerous specialists. His monographs on novæ (Nova Geminorum, 1912; Nova Herculis, 1935) remain models of their kind, and indispensable guides. They inspired in Sergei Gaposchkin, of Harvard College Observatory, a poem printed on p. 1506 of "Vistas in Astronomy", where one may read the lines:

> "And you will occupy
> In the Science of Heavens
> A perpetual niche".

Prof. Stratton is also one of the great instigators of international co-operation in science. In 1919 he participated in the meeting at Brussels when it was decided to form the International Astronomical Union, of which he was to become general-secretary during 1925–35. He has not missed a single General Assembly of the Union, and those which he organized at Leyden in 1927, at Cambridge (Massachusetts) in 1932 and at Paris in 1935 were very successful. They brought him those innumerable friendships of which he is justifiably proud and that popularity to which "Vistas in Astronomy" bears witness. It is to him that the Union owes its robust constitution and the cohesion which is its strength. With perfect tact and a profound knowledge of the behaviour of men and of nations, Prof. Stratton knows how to create about him an atmosphere of friendship and conciliation in which the spirit of co-operation blossoms naturally. He has the art of persuasion, which he exercises at a distance, adhering faithfully to the old custom of using longhand for all his correspondence: a written letter establishes far better than a typewritten one a community of thought between writer and correspondent.

When the International Union decided to create a Commission for the Exchange of Astronomers, Prof. Stratton was naturally made chairman. Thus he acquired new rights to the respect and gratitude of astronomers the world over. Nor must one forget the distinguished services which he rendered to the International Council of Scientific Unions, of which he was secretary-general during 1937–52.

Dr. Beer's plan was beautifully simple: "the purpose of the book was to present original articles and reviews, reflecting fully and critically the present situation and recent advances in astronomy and related fields . . . while the concluding paragraphs were to be devoted to a survey of unsolved questions and possible 'vistas' of future research". The length of each contribution was fixed at about 2,500 words. Naturally, some authors have followed these recommendations to the letter, whereas others have taken greater or smaller liberties with them. In fact, the length of the articles varies considerably; on average they are twice as long as the editor suggested. Since it is unlikely that anyone will read without pause, page by page, through these two large volumes, a certain variety in the form and extent of the articles presents no inconvenience to the reader; but if the foreseeable delays in publication were largely exceeded in the event, the reason lies in the unforeseen importance of the book.

The subjects treated are divided into sixteen sections: (1) co-operation and organization; (2) history and philosophy; (3) dynamics; (4) theoretical astrophysics; (5) instruments; (6) radio astronomy; (7) solar physics; (8) solar–terrestrial relations; (9) geophysics; (10) planetary system; (11) stellar astronomy; (12) photometry; (13) spectroscopy; (14) spectral peculiarities and novæ; (15) galaxies; (16) cosmogony and cosmology. It is out of the question to give an analysis here, however brief, of the contents of the different chapters, but the importance and wealth of information contained in them should be stressed. Each of the authors of the 192 monographs has discussed, according to his inclinations and temperament, a subject in which he is a leading authority. He has indicated its place in contemporary astronomy as well as its hopes for the future. Some articles are concerned with particular points, others with wider fields. It might be asked whether it would not have been advantageous to place a general article at the beginning of each section; this question presented itself to the reviewer in running through sections 12 and 13, which contain excellent studies confined, however, to specialized subjects. On reflexion it is by no means certain that the book would have gained in interest from the inclusion of such introductory articles. A third volume would have been necessary, and such heavy didactic apparatus would, perhaps, serve only to diminish in the reader the exciting impression of being launched straight away *in medias res*. Opening "Vistas in Astronomy" at random, he immediately finds there information both abundant and precise, and often hitherto unpublished; problems neatly posed; and finally, projects for research. He has thus the feeling of participating in the very life of astronomy and feeling its rhythm. Such was the

stimulating effect desired by Dr. Beer, which makes the work so much more than a 'Handbuch'.

It was inevitable that a collective work, with each author freely choosing his own subject, should present some gaps. Some are undoubtedly fortuitous, but others are due to progress in certain branches of astronomy made between the preparation and publication of the articles. Dr. Beer should not regard this as a criticism but rather an invitation to produce a sequel at some future time.

The care with which the book has been printed and the skill with which the figures have been reproduced are in the best British tradition. This fine presentation is not the least attraction of "Vistas in Astronomy".

ANDRÉ DANJON

PHYSIOLOGY OF INVERTEBRATES

Recent Advances in Invertebrate Physiology

A Symposium sponsored by the National Science Foundation; the Tektronix Foundation; and the University of Oregon. Edited by Bradley T. Scheer. Pp. vi + 304. (Eugene, Oregon: University of Oregon Publications, 1957.) 5.50 dollars.

THIS volume contains sixteen papers that formed part of a symposium held in the University of Oregon in September 1955. It gives a well-balanced survey of selected topics which have been notably developed in recent years and most of the contributions are well written and readable.

The mechanism of the nerve axon does not come in for consideration, but the neuromuscular mechanism is discussed from different angles by several authors. The review by C. A. G. Wiersma, which ranges over the main invertebrate phyla, brings out very clearly the great differences in the observable reactions to stimuli that result from slight changes in the characteristics of neuromuscular transmission, and such differences do not fall neatly into phyla. The same lesson is to be got from the account of the nervous control of insect muscles by G. Hoyle. Here there is no evidence of the inhibitory nerves familiar in Crustacea. The conception of 'fast' axons responsible for twitch-like contractions produced by single impulses, and 'slow' axons which produce a mechanical response only when a chain of impulses passes along them, is well established. These two sorts of fibres share the same end-plates, and a single axon always supplies numerous end-plates in one fibre. It is this distributed end-plate supply which enables the insect muscle to function in the extraordinary mineral environment of the insect body fluid in which the propagated action potential of vertebrates would be paralysed.

Studies on the physiology of flight muscles in insects, described by J. W. S. Pringle, have led to a satisfying picture of the possible evolution of insect flight. A large insect develops thoracic expansions, used for gliding. They can be inclined by muscular action and later folded. More powerful muscles give them a slow flapping movement to aid flight, each contraction being evoked by a nerve impulse of conventional type. Then a 'click' mechanism develops in the thorax (it is described in full in the article by E. G. Boettiger) and this leads to a sudden release of tension in the contracting muscle, causing instant relaxation, while the antagonist that is suddenly stretched instantly contracts. It is this mechanism, evolved many times independently, which makes possible the intensely rapid wing movements of the higher insects.

It is nice to have a clear account in English by H. Mittelstaedt of the 'feed-back' mechanism which ensures the accurate capture of flies by praying mantids. This makes an interesting companion piece to the review by L. M. Passano on the recognition of prey and predators by cœlenterates the co-ordinated responses of which occur in the absence of a central nervous system. 'Neurohormones' as defined by J. H. Welsh embrace both the 'neurohumors' responsible for immediate and often local reactions, and the products of neurosecretory cells which often have a prolonged hormonal action. Since the two classes of material merge into one another this is perhaps the most logical treatment.

There are many other contributions of much interest and value. For the general reader one might commend the final review by F. A. Brown, which describes the fascinating advances made by his group in recent years in defining the properties of the 'physiological clocks' by which so many living organisms regulate their lives.

V. B. WIGGLESWORTH

ELECTRO-TECHNOLOGY

Electro-Technology for National Certificate Courses

By Dr. H. Buckingham and E. M. Price. Vol. 2. (Technical College Series.) Pp. 298. (London: English Universities Press, 1956.) 12*s*. 6*d*. net.

THIS is the second volume in a series of books on electro-technology intended mainly for those students who attend the part-time National Certificate courses in electrical engineering. The general arrangement follows the same plan so that the text of each chapter not only comprises a number of fully worked examples where this is desirable, but is also supported by a set of appropriate problems to be solved by the reader. In all there are 142 well-selected problems, with answers to these in an appendix at the end of the book. The authors have included in the text a description of fifteen important laboratory experiments.

There are, however, two new features. In the first place, it is wisely based on the MKSμ_0 system of units, and secondly it contains more material than would be, or could be, covered in the *S*.2 year.

The ten chapters deal successively with units, magnetization, self-induction, mutual induction, electrostatics, generators and motors, alternating currents, resistors, reactors and capacitors, measuring instruments and illumination. There is also an appendix containing nine tables of data. The text is well illustrated with 183 figures and diagrams, with some of the illustrations depicting essential details of equipment and apparatus: a very good feature.

It is evident that this is a well-thought-out text-book based on a thoroughgoing treatment within the limitations imposed by the nature of the student for whom it is intended. Although almost all the symbols, units and abbreviations are those now generally accepted, there are still anomalies. An example of this is that although illumination is based on the candela, the foot-and-candle disease still persists, with the foot-candle as a unit of light intensity.

Few will quarrel with the quality of the contents, but many will undoubtedly consider that the authors should not have included so much material that is more appropriate to the *S*.3 year. In this way a fuller treatment and coverage could have been given to the rest.

There is a great need for text-books having a specific purpose, and in this case there is fairly general agreement as to the material appropriate for inclusion in an *S*.2 course in electrical engineering. Such text-books would have a beneficial effect on the standard of lecturing as they should eliminate or reduce the use of the chalkboard and the corresponding copying of notes by students.

In any revision of the text the author might usefully consider whether the mathematical approach is always essential as it is possible that with this type of student this may disguise or confuse the physical principles. There is some doubt whether the academic standard is not above the average reader for whom the book is intended. In particular, the approach to alternating currents could well be based entirely on the use of the rotating vector, thus leaving the trigonometrical method an applied exercise for the mathematics course.

The book is well printed on good quality paper with an attractive format and good binding. It is distinctly readable and is strongly recommended.

P. F. Soper

VOLTAGE STABILIZATION

Voltage Stabilized Supplies

Basic Principles, Characteristics and Applications. By Dr. F. A. Benson. Pp. 370. (London : Macdonald and Co. (Publishers), Ltd., 1957.) 50*s*. net.

THIS book, as stated by the author in his preface, is based on a monograph published in 1950 and most of the material of this monograph (including ninety-three figures) is reproduced with little alteration. Additional material has, of course, been added. Like the monograph the book does not deal with electromechanical devices or with the control of generators.

A large proportion (one-third) is devoted to glow-discharge tubes and their circuits. This is to be expected in view of the author's work on this subject. It would have been helpful to include manufacturers' data on the many tubes considered and one tends to be confused by the use of *CV*-numbers for valves and tubes in one section and civilian numbers in other sections. A large number of figures and graphs are given on discharge tubes but it is difficult to come to conclusions. Explanations of the practical importance of these results and suggestions for suitable tubes for various purposes would have been helpful. A most useful chapter is included on corona discharge tubes.

The two chapters dealing with thermionic valve stabilizers would be improved by the inclusion of more design data on 250–500 V. stabilizers and by the use of modern valves and tubes in the circuits and performance calculations. It should be noted (p. 169) that a shunt stabilizer valve is available for 20 kV.

A most useful chapter is devoted to battery reference sources but the work on bridges in Chapter 10 might also have been included, with advantage, in this chapter. The next chapter deals adequately with magnetic stabilizers.

The final chapter (85 pages) deals with bridge circuits, saturated diodes and miscellaneous circuits. Fig. 205 appears to be so nearly identical with Fig. 202 as to be scarcely worth including. The chapter covers an extensive range of circuits but sections tend to read as a list of published works.

Heading of the right-hand page with the title of the chapter or subject of the page would be a great improvement.

More than a thousand references are included from numerous sources and this forms a most valuable portion of the book.

Dr. Benson has been most successful in producing a well-written, clearly illustrated and valuable book for the engineer and research worker, but not quite so successful in producing a book suitable for the student.

G. N. Patchett

THE SCYTHIANS

The Scythians

By Tamara Talbot Rice. (Ancient Peoples and Places.) Pp. 255+62 plates. (London : Thames and Hudson, Ltd., 1957.) 21*s*. net.

LITTLE has been written in English about the Scythians since the late Sir Ellis Minns's great works, the second of which was published in 1942. Yet these people, who appeared suddenly as nomadic folk in the plains to the north of the Black Sea and who vanished just as suddenly as a result of the incursions of the Sarmatians, extended their influence during the period of their dominance (*c*. 700 B.C. to *c*. A.D. 50) well beyond the area of their homelands, and the characteristic art they developed still remains a joy to all art lovers to-day. It is not certain where they were cradled, the most popular suggestion being the Altai steppes, but they first appear before us as horse-breeding nomads, only now and then developing a village life. They seem to have erected no temples and we know little about their religious ideas. But they attached enormous importance to the burial of the dead and their tombs are filled with the richest of funeral furniture. Naturally, for nomad peoples wandering over vast plains, the horse was of supreme importance and value, and nearly always horses were slaughtered and buried with the dead man. There is one case where no less than 400 were so destroyed. Some of these animals were not without blemish—one could scarcely expect the living to give up all their best horses for this purpose. However, they frequently did.

Mrs. Talbot Rice has written a volume on the Scythians in a new series, "Ancient Peoples and Places", which is under the editorship of Dr. Glyn Daniel. It is an exceedingly good and readable book and is exceptionally well illustrated, both with line blocks in the text and with no less than thirty-two full pages of illustrations at the end of the work. Naturally the illustrations are concerned with the art, but one or two of the line drawings are devoted to such subjects as the plan of the Kostromskaya burial and a section at the same site. The book will fill a gap, and such a work is overdue. Doubtless the specialist in the prehistory of those regions will regret many details which the size of the volume has made it necessary to omit. But the general archæologist and the interested reader will welcome Mrs. Talbot Rice's book.

M. C. Burkitt

SCIENTISTS IN SOCIETY TO-DAY*

By the Right Hon. the VISCOUNT HAILSHAM, Q.C.
Lord President of the Council

I AM very glad to be the Minister of the Crown selected this year to propose the toast of the Royal Society. For the toast accords full well with all three Departments which it has fallen to my duty to administer in the past twelve months. Apart from its general scientific interests, the Admiralty is responsible by a strange historical chain of circumstances for the Greenwich Observatory, now established in the parish of Herstmonceux, a village known to me personally very well, but before the advent of the Astronomer Royal, possessing as it did in the Domesday Book "a priest and a wood for six Hoggs". The Ministry of Education, too, engaged as it is on its vast new programmes of teaching and awards in science and technology, would have formed a good jumping-off ground for proposing the toast of the Royal Society. Best of all, perhaps, is my present office, responsible for the Councils of Medical and Agricultural Research, the Department of Scientific and Industrial Research, and the Advisory Council on Scientific Policy. All these departments have their intimate connexions with science and their own reasons for wishing health and prosperity to the Royal Society, upon the talent of whose members they so very largely draw.

But quite apart from official interest, this toast accords also well with my own inclinations, and, as I see them, the needs of the moment. I have conned the speeches of my predecessors, and I find it has been their custom to stress the limitations of their humanism in a society of scientists, of which I, too, am a poor example.

But I would stress a point of contact rather than a point of difference. And I hope that in doing so I may be taken quite seriously even though my remarks may be couched in jocular and even facetious language. Both in Britain and the United States it is popular fashion to ridicule and condemn what the Americans call the 'egg-head', the man who from boyhood up deliberately and consciously pursues intellectual pursuits, whether humanistic or scientific (or, better still, both), with whole-hearted zest—an unbalanced fellow, they would say, a dreamy unpractical other-worldly sort of chap, unfit for the society of successful politicians, hard-headed men of business, simple soldiers, silent sailors or working journalists and all the other kind of folk who make such a botch of this practical world by refusing to think about the theoretical problems involved in the art of living.

To-night I can be as bold as brass. Although not a scientist, I am at least an 'egghead' by conviction and, I hope, by practice, and I am addressing a society of scientists who are also, always by achievement and almost by definition, 'eggheads'. It is time we got together. 'Eggheads' of the world, unite! We have nothing to lose but our brains. A country neglects its 'eggheads' at its peril. For it is the 'egghead' who is the greatest realist. It is the 'egghead' who invents the *Sputnik*, not the captain of football, nor the winner of the sword of honour, nor the president of the Junior Common Room. It is the 'egghead' who discovers penicillin, who splits the atom, who thinks of the printed circuit, the electronic brain, the guided missile in the world of science, and it is the 'egghead' on the other side of the academic fence who studies and produces the political and philosophical ideas which shake thrones, destroy empires or inspire millions of humble citizens to heights of self-sacrifice and devotion. It is the ordinary man who is the unpractical sentimentalist who dreams away three-quarters of his life in wish-fulfilment, phantasies, and leaves no trace on his generation but a nasty smell of peardrops. Therefore, I say let us be proud of our 'eggheadedness'. And let us join in a united protest to Downing Street and the White House demanding higher recognition. It is a formidable indictment of Western civilization and democracy that 'eggheadedness' is not valued at its proper worth.

When our protest is made and our just claims are allowed, as with a Government as good as this is clearly inevitable, let us remember to stress a further point of union. Let us resolve to bury for ever the divorce, almost the schizophrenia, which divides our present society (or at least our present society of 'eggheads') into two hostile and mutually uncomprehending camps—the classical humanism deriving its origin in the last resort from the culture of Greece and Rome, and the scientic world of Cavendish, Harwell and Imperial College. For the truth is that neither is complete without the other. No humanist is complete without an intimate understanding of the characteristics, the working and the potentialities of the techniques of our current scientific civilization. And I would say that no scientist was capable of giving his best unless he used the added perception he has acquired from his scientific studies to form a part of a cultured and humanized approach to life. If I may quote from a recent notable speech by H.R.H. Prince Philip, the Duke of Edinburgh: "The educated man can be a specialist or need not be a specialist, but the important thing is that his specialization, whatever it may be, should in no way prevent him from being, behaving, and thinking, as an educated man". If I may venture an example: your president, with whose name this toast is coupled, is not merely a distinguished professional chemist, but also a connoisseur of Chinese porcelain and a linguist who has addressed gatherings in Rome, Moscow and Paris in their own tongues.

Part of the trouble at least has lain in the fact that there are in the civilization of the West, of which we are members, not merely the classical lore of Greece and Rome, not merely the scientific culture of our own forebears and contemporaries, but also the living tradition of justice, integrity, compassion, love and service which we have inherited from another source, and some would say a source of divine origin. Neither classicism nor scientific brilliance, though

* Substance of the speech made in proposing the toast of the Royal Society at the 295th Anniversary Dinner on November 30.

the one may produce beauty, and the other uncover truth, is a substitute for virtue; nor can the divorce between the two be reconciled until both stand humbled at the shrine of love.

But there is one more thing which we may say together in all sincerity.

In the ideological war the scientific discipline is not merely the indispensable condition of survival; it stands four square with humanism and morality on the side of freedom.

For science, to which the work of the Royal Society is dedicated, is not primarily a subject, or a series of subjects, but an attitude of mind, and specifically the attitude of mind actuating those who seek the truth for its own sake by experiment and experience without philosophical, political or even religious preconceptions, other than the belief that the truth is there to be known, and that it can be recorded and related logically to the general body of other truths similar ascertained. Science does not give a man the faculty of knowing, or the desire for freedom, the qualities of compassion or love, or the experience of God. These are part of his eternal inheritance. But the scientist is driven by his very terms of reference to seek and publish the truth with all the single-heartedness of Galahad pursuing the Grail. Though the scientist remains as vulnerable as his neighbour to political and moral error, he is yet unlikely to accept indefinitely or corporately the political or moral indoctrination of a tyrannical system of government tied authoritatively to a body of *a priori* beliefs. Whoever retains the scientist in the employment of his society or seeks to breed a race of scientists in his schools and universities, though they may for a time neglect the humanities or despise the ordered teaching of morality and virtue, will in the end create and harbour a race of men and women rebellious against the nonsensical assumptions of a political creed unbased on human experience, and unwilling to accept as part of its natural machinery the self-adjusting mechanism of rational discussion and argument. It is this which causes me to proclaim my faith and hope in the scientist. No nation dare neglect him save at great peril; for this reason the scientist can penetrate barriers which exclude the moralist and the democratic politician. He can penetrate those barriers without political motives or even while himself suffering from political delusions, but he carries the virus of freedom in the very constitution of his being, and he cannot fail to pass it on to his new neighbours.

But here in Britain the scientist is at home, though he is, in my opinion, like other intellectuals accorded too little honour in his own country. He has been at home in Britain since Charles II formed the Royal Society not quite three centuries ago. He is at home in Britain to-day and the symbol and centre of his influence is found in your Society.

In proposing the toast of the Royal Society, coupled with the name of its president, I am thus consciously proposing the toast of a great historical institution, with its roots deep in the past, but dedicated in the present to the cultivation of a living and contemporary spirit, the spirit which is at once the especial mark and glory of our current civilization as it is to some extent the occasion of some of our deadliest perils.

PROGRESS OF CANCER RESEARCH

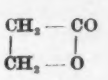
THE thirty-fourth annual report of the British Empire Cancer Campaign (11 Grosvenor Crescent, S.W.1) is a sizeable volume of nearly six hundred pages. The Campaign spent about £500,000 in 1956 supporting research at some thirty centres, in addition to financing more than sixty individual investigators.

The work described in the report can be classed conveniently in three main branches. First, studies of human tumours and clinical investigation (including diagnosis, prognosis, and the evaluation of therapeutic measures); secondly, radiology, which includes physics of radiations, radio-therapy and radio-biology (namely, action of radiations on tissues, cells, macromolecules and other substances of biological interest); and finally, the largest class, which embraces: (1) Carcinogenesis and carcinogens. (2) Environmental cancer, in particular the relation between smoking and lung cancer, which is the most interesting topic in cancer research at the present time. Some experts are convinced that environmental research, which uses demography as its principal theme, is to-day the most hopeful way of attacking the cancer problem. It does not yet occupy a very prominent position in the studies catalogued in the report because very few, if any, of the young scientists qualified to take part in, say, work on nucleoproteins have any interest in, quite apart from training or capacity for, research on environmental, demographic and statistical lines. (3) Carcinogenic viruses. (4) Biochemistry of tumours; including the application of tracer compounds to the study of tumour and tissue metabolism, and the factors which affect tumour growth. (5) Enzymes. (6) Hormones. (7) Nucleic acids. (8) Cytology and cytochemistry. (9) Steroids. (10) Immunology. (11) Chemotherapy. (12) Tissue culture. (13) Genetics.

Some passages are highly technical and could perhaps be described in Baedeker's terms as "for adepts only, with steady heads". Parts of the report might be regarded as inflated with unnecessary detail, while other sections dismiss in a few lines what has in fact demanded several years of disciplined study and laboratory technique: this helps to explain why the task of the reviewer, in deciding what to put in and what to leave out, has a subjective element.

With regard to carcinogens, the latest advances seem to be that certain comparatively small molecules, and quite well-known compounds, have been revealed as possessing carcinogenic activity or able to 'initiate' carcinogenesis (stage 1 on the Berenblum theory) or 'promote' it (stage 2) once the first step has been overcome by an initiator. The standard carcinogens, benzpyrene, etc., can accomplish both

stages. β-Propiolactone (I), ethyleneimine (II) and cholesterol have been shown to be carcinogens; urethane induces carcinogenic changes when it is given by mouth to mice, for not only do lung cancers develop but cancers of the dorsal skin are initiated—tumours appearing in this area after painting with croton oil. Phenol has been found to have strong 'promoting' activity and weak total carcinogenic potency. An important feature of the assay for tumour-inducing activity is the variation of response due to differences in susceptibility in the experimental animals. For example, Rusch (United States) is quoted (p. 193) as reporting that "almost as many tumours were produced when croton oil, phenol, iodoacetic acid, or allylisothiocyanate, were applied alone, as after treatment with DMBA. However, croton oil applied alone to mice of another strain produced no tumours".



(I)

(II)

Salaman and colleagues find that croton oil is a powerful promoter, but a weak complete carcinogen and only for sensitive strains of mice. These workers have bred strains of mice varying widely in response when treated by one application of dimethylbenzanthracene followed by painting with croton oil ("Strain 101—high and homogeneous susceptibility; strain *AKR*—moderate, variable susceptibility; strains C_3H, $C_{57}Br$ and *A*—no tumours produced.") Such differences of sensitivity could explain the discrepancies between the results of tests for potency when different laboratories are working with carcinogenic agents of low intensity; of course if mouse tissues are treated with an excess of powerful carcinogen, susceptibility differences become obliterated. These facts should still the storm-in-the-teacup raised by the failure of workers in Britain to confirm the positive results of Wynder (United States) on the tumour-inducing activity of tobacco tar on mouse skin. It might perhaps be pointed out that the lack of carcinogenic response of some mouse skin to tobacco tar does not *prove* that it must therefore be inactive on human lung tissue (pure benzpyrene, for example, is highly carcinogenic for mouse skin but far less so for rat skin or for rabbit skin).

The report includes an interesting account of a visit to Wynder's laboratory and to other important centres of cancer research in the United States.

A large number of experiments are still being devoted to the nucleoproteins of tumours and normal tissues, chiefly with the aid of tracers; details of more than thirty such studies are included in the report. Investigation of nucleoproteins is fundamental to the biochemistry of living matter but no great advance in cancer research has yet been made from that angle, and it might perhaps be questioned whether the attack from this basic level is not too academic an approach.

The immunological aspect of neoplasia, which has always attracted great interest from the earliest days of cancer research, has received an increasing volume of study in the past few years. Some of this work has lately been expressed in very difficult terminology, theories being offered without adequate observations in support. One such exponent is now beginning to take up a rather more critical point of view; he writes (p. 292): "However, as with all reported cancer differences, the difficulty of isolating an exactly comparable control normal tissue makes firm interpretation difficult. Moreover, it is always possible to object that antigenic simplification, if found, is an expression of the immaturity of the cancer cell and not primarily of the malignant state. The most convincing evidence would be to discover new facts predicted by the theory".

Research on the sex hormones and related steroids has encountered something of a setback, temporarily no doubt; one of the leading authorities (after an extended account of a "Symposium of Oestrogen Methodology" and a very competent study of "The Excretion of Steroids in relation to Neoplastic Disease") concludes that (p. 501): "The excretion pattern of the remaining twenty cancer patients, all of whom had large neoplastic growths, did not differ significantly from normal and it cannot be assumed that the abnormal pattern, when it occurs, is primarily a result of the neoplastic growth. The results do not support the idea of a specific urinary steroid excretion pattern associated with neoplastic disease".

Chemotherapy received slightly less emphasis this year: the efforts put into this line of work have in the past been nothing less than heroic. The American laboratories have by no means given up hope: on the contrary, it is said that they are embarking on an immense scheme of screening tests for cancer chemotherapy, involving something of the order of a million mice.

Tissue culture seems to be moving up in the hierarchy; a dozen studies are outlined in the report and it is good news that tissue culturists are at last becoming aware of the possibilities of Earle's discovery, about 1943, that normal mouse fibroblasts growing *in vitro* can become transformed spontaneously to malignant cells in the absence of carcinogens; this discovery is re-stated in two places in the report.

The work being carried out in the various medical physics laboratories mentioned in the report indicates that the age of automation is coming closer in research as in industry. In view of the widespread shortage of trained physicists it seems profitable for those who are working in this field to produce methods and instruments designed to reduce the time spent in routine calculations; and in the study of the distribution of radiation within patients being treated either by X-irradiation or with radioactive isotopes. In one centre the possibility of the application of electronic computing to routine problems of treatment is being considered, and in another generalized distribution charts regardless of the contours of the individual patients have been produced. Automatic scanners are also being designed for the localization of radioactive sources in patients or on chromatograms and also in the form of scanning X-ray tubes. X-ray tubes in their turn may be superseded by radiography with radioactive sources and a detailed study is being made of xenon-133 for this purpose. This isotope can be produced as a fission product or by direct irradiation of xenon gas. Determination of the physical factors of xenon-133 is complicated by the presence of other isotopes of xenon. In practice, good radiographs of fractures of the wrist and ankle can be obtained with exposures of only a few seconds using sources of high activity. In the treatment of

malignancy, more and more emphasis is being placed on the use of cobalt-60 and cæsium-137 units containing kilocurie amounts and on the use of the linear accelerator. As a consequence of this an immense amount of work is being done on their dosage distributions and on the properties of the radiations produced. This in turn requires the design and production of dosimeters suitable for the accurate measurement of beams of this quality. Calorimetric methods are reported from several centres, including the microcalorimetric method of measuring beamed radiation using thermistors to measure the temperature rise in lead absorbers. The development of 'Perspex' dosimeters for measuring high dose-rates in an electron beam is also discussed. At the other end of the scale it has been found that sealing a solid or liquid sample in intimate contact with a phosphor within a plastic sheath provides a simple and easy method for estimating alpha-ray activity in very weak alpha-emitting substances.

As the population as a whole becomes more and more 'radiation conscious' it is important that the effect of low levels of radio-activity applied to large populations should be studied as well as the techniques for general protection of workers dealing with what may prove to be dangerous amounts of activity. Some of the main hazards to the latter are those relating to handling metals, which may become fixed in bone with subsequent irradiation of that bone and the consequent risk of irradiation-induced neoplasms. The investigation of certain chelating agents as an aid to the removal of these radionuclides is reported. Film-badge monitoring using different types of film holders is now widely used and in many centres the continuous wearing of film badges is obligatory for all staff likely to be exposed to any ionizing radiations. The development of a whole-body gamma-ray monitor for measuring the body burden in case of the accidental ingestion or inhalation of radioactive substances is proceeding. From Australia comes a report of the variation in the radioactivity of rain-water which has been correlated with tests of atomic weapons at the testing range some 600 miles away.

There is not a great deal of special note in the field of cancer morphology. Experience with the diagnosis of cancer of the cervix by exfoliative cytology is reported from two centres, the most detailed and provocative coming from Birmingham. Among 4,000 gynæcological out-patients fifty-three cases of cancer of the cervix were recognized by ordinary clinical methods. To these, cytological examination added three cases of frank invasive cancer and fourteen of carcinoma *in situ* or pre-invasive cancer. At the same time there were twenty-two false positive and three false negative reports. The 'pick-up' rate is low in this series, and Prof. H. C. MacLaren doubts whether the method justifies its cost except for research purposes. The Newcastle figures, however, show twenty-one invasive cases and fifteen carcinomata *in situ* 'picked up' in 2,500 smears. Such differences probably reflect differences in the material submitted, which might be related to geographical or social difference in the incidence of cancer of the cervix, or more probably differences in the type of clinic involved and the efficiency of its screening procedure. It is, however, also possible that they reflect differences in the efficiency of the cytologist, or in their criteria of abnormality, or even differences in the histological criteria of invasiveness which are the ultimate standards by which the accuracy of the cytologist's diagnosis must be judged. There has been some criticism of the use in Birmingham of a cytologist without medical qualification in charge of the reporting of smears, but it is most improbable that this is the cause of the low 'pick-up' rate. In any event, if the method is ever to become economically possible on a large scale, it will have to be organized in some such way as this. These comparatively unfavourable figures from Birmingham need not perhaps be taken too seriously, but they sound a necessary warning against too uncritical acceptance of the worth of cytological screening in cancer of the cervix.

Dr. P. M. F. Bishop (Guy's Hospital) reports a laborious investigation which seems to brand as a fallacy the long-held view that therapeutic œstrogen may be a significant factor in the production of cancer of the uterine body or the breast. Of 420 cases known to have been so treated, followed up for 4–20 years, only one had developed endometrial cancer. Follow-up of cases with presumed high endogenous output of œstrogen, and retrospective survey of the previous œstrogen treatment of cases of endometrial cancer, gave equally non-significant results.

The work of the Cancer Register recently established at Kampala, Uganda, continues, and it is to be hoped that it will soon be making a major contribution to the many problems raised by the distribution of different types of cancer in Africa. This year's harvest is, however, limited to observations on bone changes in Kaposi's sarcoma, and on jaw tumours in Africans. The latter reach the remarkable figure of 5·6 per cent of all tumours seen at Kampala, the commonest kinds being sarcoma (type unspecified, but not osteosarcoma or osteoclastoma), adamantinoma, carcinoma, and mixed salivary tumour of the palate. An international conference on cancer of the liver was held at Kampala in 1956, but the survey of its findings presented in the report is too brief to be very illuminating: the most important point that emerges is that in the absence of any generally agreed definition of cirrhosis the criteria used in the pathological diagnosis of that condition vary so greatly from place to place that comparative statistics of the incidence of cirrhosis, and thus of the relation of cancer to cirrhosis, in different parts of the world are of very little value at present.

These annual reports would be greatly enhanced in value by a subject index. They present a unique compendium of information on current research in very many fields more or less directly related to cancer. However, they are arranged geographically, by departments, rather than in any logical order, and it is not easy to assemble all the aspects of one problem. The summary with which the volume begins acts as a guide to its contents, but it makes a poor preface, for it is so impartial and comprehensive that it is nearly unreadable. A thoughtful preface with some attempt to sum up the year's progress and direct attention to its main achievements would form a better advertisement of the aims and policies of the Campaign and a far more attractive introduction to its report, while its function as guide might well, as suggested, be far better performed by an index. It is very noticeable that an account by Sir Ernest Kennaway of a visit to the United States to discuss tobacco and lung cancer is the least formal article in the report, and also the most readable.

POLYMORPHISM IN PLANTS, ANIMALS AND MAN

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At all stages of plant evolution polyploidy and changes in the content of the chromosome-set have played a decisive part in the supply, and indeed in the control, of heritable variation. Their analysis into a unified concept of chromosome-genetics is due principally to Darlington[1]. A corresponding study of the animal kingdom is not as yet available. For many reasons, which include the rarity of asexual reproduction and self-fertilization, it is likely to provide a less-definitive picture, but it remains an outstanding need. For against such a background the Mendelian phenomena must be set, and it is they which supply the bulk of heritable diversity within freely interbreeding populations. This is controlled in three principal ways, the significance of which is not always fully appreciated even by geneticists, certainly not by biologists in general. That is to say, it may be : (*a*) polygenic ; (*b*) the result of major genes eliminated by selection and maintained in the population by recurrent mutation ; or (*c*) polymorphic.

Polygenic qualities, such as human height, are due to the action of a large number of genes having small, approximately similar and cumulative effects. These, of course, interact with environmental differences, as in all genetic variation.

When, on the other hand, a major gene mutates, the new allelomorph will generally be disadvantageous. The reasons for this are sufficiently obvious. Mutations are random changes relative to the needs of the organism, and when these occur within any highly organized system (and such is the body of an animal or plant), they are more likely to be harmful than useful. Now the genes have multiple effects. It would indeed be difficult to suppose that the chemical and embryological processes connecting a gene with a particular character should in no way modify the general development, whether or not the end result in question is of importance. Thus all the major genes studied in *Drosophila melanogaster*, though normally identified by their influence on such apparently trivial qualities as wing-venation or eye-colour, react upon the viability (length of life, vigour or reproductive capacity) of the fly. They must, therefore, affect the physiology of the organism and, from what has just been said, usually in an unfavourable way.

In polymorphism, on the other hand, we are concerned with the fate of initially advantageous major genes. Logically, one must also envisage the situation in which a mutant gene is neutral as regards survival value. However, Fisher[2] has shown that the balance of advantage and disadvantage between the allelomorphs concerned must be extraordinarily exact to produce that situation. Therefore, such selective neutrality is both rare and of short duration. For the frequency of such a gene can have increased but little by mere chance before the delicate balance required for its neutrality is upset by changes in the environment or in the gene-complex of the organism. Thus if a character controlled by a major gene occupies even 1 or 2 per cent of a population, then that gene must have some advantage.

Polymorphism was defined by Ford[3] as the occurrence together in the same habitat of two or more discontinuous forms of a species in such proportions that the rarest of them cannot be maintained merely by recurrent mutation. That is to say, it excludes geographical races, rare disadvantageous mutants and continuous variation falling, for example, within a curve of normal distribution and controlled by polygenes. It arises in the following way. Mutation, though very rare, is a recurrent phenomenon, so that genes are given opportunities, repeated at long intervals, for success or failure. Any one of them will begin to spread if since its previous origin as a mutant its effects have acquired an overall advantage owing to a change in the environment or in the average gene-complex of a population. Yet it is very improbable that all the results of its action will be useful since these are diverse and, as already noticed in another connexion, the chance of fitting each of them harmoniously into the highly organized system of the body will be remote. Those favoured by selection will become dominant and those opposed by it will become recessive, these processes occurring with increasing rapidity as the gene-frequency rises. Thus the heterozygote will come to have none but favourable effects and will be at an advantage compared with both homozygotes, each of which will evoke some desirable and some undesirable qualities[4].

Consequently, the spread of a major gene will frequently generate a polymorphism, in which distinct genetically controlled forms will reach an equilibrium in the population. They will do so when the advantage of the heterozygote is balanced by the disadvantage that it fails to breed true. Thus it is to be noticed that the heterozygote is bound to gain a superiority, in itself sufficient to produce polymorphism, even when a balance of contrasted types is ensured ecologically. Thus the Batesian mimicry of butterflies, in which relatively palatable species obtain protection by copying those which are relatively distasteful, tends to produce polymorphism. It does so because the advantage involved wanes and is converted into a disadvantage as the numbers of a mimic increase relative to those of its model. Selection then favours the evolution of several distinct forms under genetic control, and these should become stabilized at such proportions that they all receive equal protection : indeed, we find that their relative abundance varies from one locality to another in relation to that of their respective models. This situation in itself generates diversity within the population ; yet, in addition and providing as it were a double basis for polymorphism, the heterozygotes are at an advantage compared with their corresponding homozygotes—a condition which also supplies all that is needed to maintain a polymorphism.

Mimicry is perfected by selection operating upon the gene-complex, within the ambit of the major

gene which acts as a switch-mechanism. It does so just as, at a different genetic level, the characteristics of each sex are open to gradual evolution, though subject also to a switch-control deciding whether the individual be male or female.

The most striking instance of evolution ever actually witnessed is that of 'industrial melanism', in which blackish forms of more than sixty species of moths have been, or are, spreading in the industrial areas of Britain and elsewhere. They are under direct genetic control, the black phase being almost invariably a simple dominant. These species are all cryptically coloured and derive protection from active predation by birds owing to their resemblance respectively to pale bark and lichen in the normal countryside, and to the blackened tree trunks in the areas polluted by smoke[5,6a]. Yet in view of what has already been said, we should expect this distinction to involve physiological as well as visible changes, and evidence is already accumulating to indicate that the (melanic) heterozygotes are hardier than the normal pale forms[5b,6].

We are here witnessing the rapid spread of a gene (transient polymorphism) in response to a cataclysm unparalleled heretofore: the effect of industry upon the countryside. In numerous manufacturing districts the melanics have reached 95 per cent of the population (a gene-frequency of 77·6 per cent assuming equal viability of the genotypes, but somewhat less in view of the superiority of the heterozygotes) and even up to 98 per cent. Yet we are not to suppose that the genes responsible for them will anywhere spread until their once 'normal' allelomorphs are maintained solely by mutation pressure, giving rise only to one pale specimen in many thousands. On the contrary, they should now pass from a 'transient' to a true or 'balanced' polymorphism, in which the frequencies of the allelomorphs will be maintained by contending selective advantages and disadvantages.

In both mimicry and industrial melanism the features by which polymorphism is recognized are of obvious selective importance. They may, on the other hand, be of no apparent significance, but we cannot, therefore, suppose that the genes controlling them are of neutral survival value. Indeed, we can be certain that this is not so. One type of evidence which may be used for substantiating that view can be illustrated from work on the Scarlet Tiger moth, *Panaxia dominula*.

An isolated colony of that insect at Cothill, Berkshire, is polymorphic for a small variation in colour-pattern. The heterozygotes, though recognizable, have usually to be examined carefully to reveal it, but the rare homozygotes are much darker than the normal form and consequently are relatively conspicuous when at rest. This colony has been more fully quantified than has any other population of animals upon earth. The species is single brooded, and at Cothill the numbers have been estimated each season for many years by the method of marking, release and recapture. At the same time, since all three genotypes are distinguishable, the gene-frequency of the polymorphism concerned has been ascertained.

It is possible to calculate to what extent a change in the ratio between a gene and its allelomorph can occur by chance provided the gene-frequency and the size of the population be known[7]. In this instance, both these requirements are fulfilled, and it can be shown that the observed fluctuations in the polymorphism ratios are too great to be fortuitous: they must be the result of selection, changing in intensity and in direction from season to season[8,9]. That is to say, we have evidence that, as deduced by theory, the genes controlling this polymorphism, trivial as it appears, are of importance to the species, being subject to selective advantages and disadvantages.

In the example provided by the Scarlet Tiger moth, polymorphism appears principally to be maintained by selection operating upon qualities other than those which are visible. But even such superficial features are not always available for its recognition. The variation involved is then *concealed*, and in such circumstances apparently similar individuals differ from one another in ways affecting their viability which, although important, can be detected only by cytological or physiological means. Yet the genes responsible for it segregate and contribute to the variable background against which the environment as well as other genes operate. Such concealed polymorphism is therefore bound to influence some of their effects.

In many species of the fly *Drosophila* numerous chromosome inversions can be recognized. This situation has been analysed with much success by Dobzhansky[10] working especially upon *D. pseudoobscura* and *D. persimilis*. He finds it possible to identify certain inverted segments, a considerable series of which is known especially in the third chromosome. Since their frequencies vary characteristically in natural populations, both from place to place and cyclically from one time of year to another, it is evident that they are balanced by contending advantages and disadvantages. This is substantiated by laboratory experiments, demonstrating that the relative superiority of one compared with another gene-arrangements varies, for example, with temperature. As is to be expected, heterozygous inversions are favoured compared with either of the homozygotes, so maintaining diversity and providing a reserve of adaptations to meet different sets of conditions. But the various types, important as they are, can be distinguished only by cytological means; except in that known as 'sex ratio', which causes the *X*-chromosome in males to divide twice at meiosis and the *Y* to be lost, so giving rise almost exclusively to female progeny[11]. Thus these inversions generally constitute a concealed polymorphism. The controlling unit here is not a single gene but a group of closely linked genes acting as a switch-mechanism; that is to say, a super-gene[12].

From the functional point of view the inversions, reducing as they do crossing-over between unlike segments, serve to hold together those genes which co-operate to produce useful effects. It may well be inquired why these should chance to occur near one another on the same chromosome so that they can be included within an inverted segment. The answer is that their proximity has been *evolved*, and here we reach a concept of importance in polymorphism as a whole. If two or more genes interact favourably it will be advantageous to keep them together, just as it will be to transmit in a block a gene and those 'modifiers' which improve its effects. Apart from any other counterbalancing disadvantages which may be involved, selection, therefore, will favour those translocations which bring such genes into the same chromosome and, afterwards, such mechanisms as prevent their scatter: it does so by reducing crossing-over between them. This may be achieved by inverting a segment containing them, but that is

not the only means available: alternatively, there may be a direct reduction in the chiasma-frequency rearrangements. Even if the genes in question should initially be on the same chromosome by chance, their adjustment to give favourable chromosome-types must be due to selection. In general, it may therefore be said that there is a tendency for the unit controlling a polymorphism to evolve from a single major gene to a super-gene.

That conclusion doubtless applies to the examples already mentioned. Two of them, the polymorphism of *Panaxia dominula* in one isolated colony, and the phenomena of industrial melanism, are probably too recent for it to be detectable. However, the work of Clarke and Sheppard is at last beginning to throw light on the genetics of butterfly mimicry, and they inform me that several of the mimetic forms of the African *Papilio dardanus* behave as if controlled by multiple allelomorphs. This, as they fully realize, is suggestive. For very close linkage can give the effect of allelomorphism or an approach to it.

However, apart from the theoretical necessity of that concept, the control of polymorphism by means of super-genes is not in doubt; we can examine the process both when complete and during its evolution. Before proceeding further, it is worth while to quote instances in which these stages can be detected in lower organisms.

The polymorphism of heterostyly became famous when Darwin studied it in the primrose and the cowslip[13]. In these species the flowers are of two types. They are about equally common and are borne on separate plants: that is to say, 'thrums' with anthers at the top of the corolla tube and the stigma at the bottom, and 'pins' in which the positions of these floral parts are reversed. Moreover, thrums have larger pollen grains than pins; they have also a stigma of a different shape and with shorter papillæ. This diversity provides an outbreeding mechanism because, as Darwin showed, cross-pollination by insects can occur more easily between dissimilar (pin and thrum) than similar flowers. He recognized also that its effects are enhanced by differences in fertility. For even when crossing between like types takes place, it is a relative failure: pollen produced by a pin plant requires the environment provided by the female parts of a thrum flower for successful growth, and the reverse.

Thrum behaves as a simple dominant to pin, but the crossing of unlike types in natural conditions ensures that the thrums are normally heterozygotes. The genetic switch-mechanism involved is, in fact, that of a super-gene: a group of very closely linked genes controlling pollen-size, anther-height, style-length and type of stigma. Crossing-over between them is very rare. When it does occur it can separate and interchange the constituent units, so producing short homostyles and long homostyles. In the latter, the male parts are those of a thrum flower and the female parts those of a pin; thus the anthers clasp the stigma at the top of the corolla tube. This type is therefore fully self-fertile as its selfing is equivalent to a cross between a pin and a thrum. The result is an inbreeding mechanism which can be substituted for the outbreeding one of heterostyly when the evolutionary stituation demands it, and this is in fact happening in two districts in southern England to-day[14].

In the heterostyle–homostyle mechanism, which naturally is widespread among plants, the evolution of the super-gene mechanism seems generally to be perfected. A stage in its production is illustrated by the snail *Cepaea nemoralis*, in which Cain and Sheppard[15] have demonstrated with great success the working of natural selection. The species is polymorphic both for colour and banding. Yellow shells are recessive to those of the brownish shades while the possession of bands is recessive to their absence. Yellow shells are less conspicuous upon light soil as on a chalk down, and upon green herbage, and in such localities they are relatively common. The brownish shells are the better concealed in a beech wood and upon dead vegetation in general, and here it is they which predominate. Similarly, the banded shells have an advantage upon a diversified background, such as a mixed hedgerow, and the plain upon a more uniform one. The shells are preyed upon by thrushes which carry them to favourite stones where they break them open, and in each type of habitat the remains contain an unduly high proportion of the inappropriately coloured and banded forms: the birds are, in fact, powerful selective agents.

We may feel confident it is not fortuitous that there is linkage between the two pairs of allelomorphs concerned. The cross-over value between them may be as high as 20 per cent, yet there is evidence that the amount of linkage varies significantly in different populations[16]. This is exactly the situation which could lead to the formation of a super-gene. One of the great needs in genetic research at the present time is to study the evolution of close linkage by means of selection experiments, and *Cepaea nemoralis* exemplifies the type of material required for that purpose.

There is yet another way in which linkage affects polymorphism. One of the commonest forms of mutation is that producing recessive lethals or semi-lethals. These accumulate in the immediate neighbourhood of the controlling gene or super-gene owing to the high frequency of its heterozygous genotype in which, as recessives, they remain protected from selection because in single dose. Only when they are sufficiently far along the chromosome to be at all often separated from the switch-unit by crossing-over will they lose the shelter it affords. Clearly such linkage must magnify the already-mentioned superiority of the heterozygote but in respect only of one of its homozygous genotypes: that is to say, the 'dominant'. The disadvantage of the other is ensured by the absence of the quality for which selection is operating.

It is for this reason that dominant polymorphic traits are so frequently reported as 'linked with a lethal'. A well-known example is provided by the white female phase of the butterfly *Colias philodice*, in which it is difficult to establish a strain of homozygous whites for this reason[17].

The features of polymorphism here described are general principles applicable wherever that condition is found, as are the far-reaching deductions to which they lead. They can therefore be extended to the human race, for man is one of the most polymorphic animals known.

When the blood groups were first treated as examples of balanced polymorphism[18], the significance of that step did not at once attract attention though it received emphatic approval from R. A. Fisher. In fact, some time elapsed before it gained any wide acceptance: even after ten years Dobzhansky[19] could see no reason to regard the blood-group genes as

of other than neutral survival value. Yet theoretical considerations inevitably demonstrate the contrary and show that they must be maintained in the population by contending advantages and disadvantages: so does their occurrence in the great apes, indicating a diversity long continued. Indeed, it was suggested by Ford, in March 1940, that these genes must have unknown effects for which they are selected[2] even before the discovery, by Levine and Katzin in October of that year, that dangerous rhesus incompatibility can arise between mother and fœtus[19].

The concept of polymorphism when applied to man leads to further deductions in the field of serology. Since the blood group genes must have multiple effects, favourable and unfavourable, by which they are balanced, they are bound to influence the general physiology, and in such a way as to produce characteristic responses to stimuli of various kinds and to the onset of changes in the body. Ford[20] therefore pointed out that individuals belonging to the different blood groups would not be equally susceptible to certain specific diseases. That prediction was confirmed six years later when Struthers[21] discovered that a larger proportion of group *A* than of group *O* babies die of broncho-pneumonia during the first two years of life. The results are fully significant but require to be corroborated on further sets of data. Aird, Bentall and Fraser Roberts[22] then showed that a significantly high proportion of those who suffer from cancer of the stomach belong to blood group *A*. An important further step was taken when Clarke *et al.*[23,24] demonstrated that duodenal ulcer is unduly common both in individuals belonging to group *O* and in those who fail to secrete the *ABO* antigens into their saliva. This latter condition constitutes another polymorphism. It is controlled as a simple recessive and in Britain affects about 22 per cent of the population, while the remainder of the community secrete these substances in large quantities. Further work along these lines is revealing other associations between pathological states (for example, pernicious anæmia, fracture of the hip in old age) and the different *ABO* blood groups.

So far such investigations have largely been confined to that series, owing partly to a deplorable lack at the present time of most of the other sera (except those of the commoner rhesus types). When the necessary facilities are available, it should be possible also to detect correlations between other groups and the incidence of certain diseases. This indeed should be demonstrable for all forms of polymorphism, including the newly discovered human 'physiological' types. For example, nodular goitre patients include a significant excess of those unable to taste phenylthio-urea[25] (confirmed by Clarke *et al.*, in the press). That compound is intensely bitter to about 70–80 per cent of the population in Europe and the Near East and tasteless (except in large concentrations) to the remainder. In this curious diversity the inability to taste is a simple recessive, subject to minor complications due to modifiers. It also exists as a polymorphism among anthropoid apes[26]; a fact which suggests that it has been maintained from a remote and pre-human period.

The value of the blood groups in anthropology has been recognized for nearly forty years but, at least until recently, for the wrong reason. By a curious inversion of logical thought, it was held that their occurrence in distinct and characteristic proportions in the different races of mankind was specially important because the variation involved was selectively neutral. Precisely the contrary is true. The fact that the genes concerned are balanced by selection at optimum frequencies, which differ from race to race, is the one which gives them significance as a criterion of relationship. It does so because in these circumstances their proportions are influenced by the average genotype of the population in which they occur.

Applying the theory of polymorphism to human examples, we can be sure that in man the heterozygotes are at an advantage compared with the homozygous types. Not only has this been demonstrated in one noteworthy group of instances but also in them the nature of that advantage has been revealed[27].

Sickle-celled anæmia is the homozygous expression of a gene which merely produces the innocuous sickling 'trait' when heterozygous. In the homozygotes, the normal hæmoglobin is replaced principally by an abnormal type, but up to 20 per cent of the ordinary fœtal hæmoglobin may also be present. This leads to the formation of irregular 'sickle-shaped' red corpuscles and produces hæmolysis severe enough to cause an extreme and generally fatal anæmia. Indeed, the fertility of this genotype is less than one-quarter that of the heterozygotes. These latter are quite healthy, but their hæmoglobin consists of the normal and abnormal types in approximately equal quantities. Their red corpuscles are unaffected while in circulation but they assume the sickle-shape, though to a less extreme degree, if the oxygen tension of a drop of blood be lowered by the use of ascorbic acid or by other means. Thus the heterozygotes can be identified. Though generally absent or of extreme rarity, they constitute a considerable proportion of the population in a few regions, and they amount even to 40 per cent in some African tribes. Evidently in these places, and there alone, they possess an advantage so considerable as to outweigh the heavy destruction of the homozygotes. The nature of this has been discovered[28], for the sickling trait confers marked immunity to subtertian malaria. The polymorphism is established only where that disease is common; for there the heterozygote is favoured compared with either homozygote, so ensuring diversity.

A glance at any work on the human blood groups will show that several of them are controlled by a switch-mechanism already identified as a group fo closely linked genes. That is to say, the expected evolution of super-genes has taken place in man. In other instances it may be so complete that it has not yet been distinguished from allelomorphism: a situation which may be true of the well-known *ABO* system itself.

It has already been pointed out that there is great need to study the evolution of linkage and of supergenes experimentally. Possibly those processes can be examined in another way: by observing their occurrence in human populations. Two opportunities for doing so may be mentioned here. The first is provided by the Henshaw blood group, which is principally found in African Negroes. The gene controlling it is extremely closely linked to that responsible for the well-known *MNL* groups, but in a way which differs in different regions: for in West Africa, but not elsewhere, the Henshaw gene is always carried in the same chromosome with that producing group *N*. Secondly, there is good, though perhaps not

decisive, evidence that the genes controlling the Lewis and Lutheran groups are near one another on the same chromosome (a cross-over value of 5·6 between them has been assessed). They might show different degrees of linkage if examined in widely separated human races.

The theory of polymorphism is a logical deduction from the facts of particulate inheritance, especially as analysed by R. A. Fisher. It has been extended and developed from a study of lower organisms, in particular the Lepidoptera. The association of the blood groups with specific diseases was predicted in advance of its discovery because it follows as a consequence of that theory. Its verification is opening up a new branch of medicine the results of which may be of value in diagnosis and conceivably in treatment.

[1] Darlington, C. D., "Chromosome Botany" (Allen and Unwin, London, 1956).
[2] Fisher, R. A., *Proc. Roy. Soc. Edin.*, **50**, 204 (1930).
[3] Ford, E. B., in "The New Systematics", 493 (Oxford, 1940).
[4] Sheppard, P. M., *Symp. Soc. Exp. Biol.*, **7**, 274 (1953).
[5] Kettlewell, H. B. D., *Heredity*, **9**, 323 (1955).
[5a] Kettlewell, H. B. D., *Heredity*, **10**, 287 (1956).
[5b] Kettlewell, H. B. D., *Proc. Roy. Soc.*, B, **145**, 297 (1956).
[6] Ford, E. B., *Ann. Eugen.*, **10**, 227 (1940).
[7] Fisher, R. A., "The Genetical Theory of Natural Selection" (Oxford, 1930).
[8] Fisher, R. A., and Ford, E. B., *Heredity*, **1**, 143 (1947).
[9] Sheppard, P. M., *Heredity*, **6**, 349 (1951).
[10] Dobzhansky, Th., "Genetics and the Origin of Species", 3rd edn., 156 (Columbia, 1951).
[11] Darlington, C. D., and Dobzhansky, Th., *Proc. U.S. Nat. Acad. Sci.*, **28**, 45 (1942).
[12] Darlington, C. D., and Mather, K., "The Elements of Genetics" (Allen and Unwin, London, 1949).
[13] Darwin, C., "Forms of Flowers" (Murray, London, 1877).
[14] Crosby, J. L., *Evolution*, **3**, 212 (1949).
[15] Cain, A. J., and Sheppard, P. M., *Genetics*, **39**, 89 (1954).
[16] Fisher, R. A., and Diver, C. D., *Nature*, **133**, 834 (1934).
[17] Gerould, J. H., *Genetics*, **8**, 495 (1923).
[18] Ford, E. B., "Genetics for Medical Students" (Methuen, London, 1942).
[19] Levine, P., and Katzin, E. M., *Proc. Soc. Exp. Biol. and Med.*, **45**, 343 (1940).
[20] Ford, E. B., *Biol. Rev.*, **20**, 73 (1945).
[21] Struthers, D., *Brit. J. Soc. Prev. Med.*, **5**, 223 (1951).
[22] Aird, I., Bentall, H. H., and Roberts, J. A. F., *Brit. Med. J.*, ii, 799 (1953).
[23] Clarke, C. A., *et al.*, *Brit. Med. J.*, ii, 643 (1955).
[24] Clarke, C. A., *et al.*, *Brit. Med. J.*, i, 758 (1957).
[25] Haldane, J. B. S., "The Biochemistry of Genetics" (Allen and Unwin, London, 1954).
[26] Fisher, R. A., Ford, E. B., and Huxley, J. S., *Nature*, **144**, 750 (1939).
[27] Allison, A. C., *Symp. Quant. Biol.* (Cold Spring Harbor), **20**, 239 (1955).
[28] Allison, A. C., *Ann. Human. Gen.*, **19**, 39 (1954).

SCIENCE OF METALS AT OXFORD

AT a meeting of Congregation held on November 5, the University of Oxford accepted with gratitude the generous gift of £65,000 made by Mr. Isaac Wolfson to establish a professorship in metallurgy, and by a decree passed on November 19 Dr. W. Hume-Rothery, of Magdalen College, was elected as the first Isaac Wolfson professor, with effect from January 1, 1958.

Metallurgical research work at Oxford was started by Dr. Hume-Rothery in 1926 in temporary accommodation provided by the late Prof. W. H. Perkin. After a few years, the subject was transferred to the Inorganic Chemistry Laboratory where one, and later two, rooms were made available by the late Prof. F. Soddy. Working with one or two research students, a series of papers on copper, silver, and magnesium alloys was published. Later, owing to the continual interest of Professor (now Sir Cyril) Hinshelwood the laboratory accommodation was gradually increased, and a lectureship in metallurgical chemistry was awarded in 1938. During the Second World War, the research work was extended to include the structures of ternary and quaternary alloys of aluminium, and alloys of transition metals were also studied. Although lectures were given, metallurgical work remained a postgraduate research subject until 1949, when metallography was added to the list of supplementary subjects in the Final Honour School of Natural Science.

Metallurgical work at Oxford received a great stimulus when in 1954 the George Kelley readership in metallurgy was endowed by the Pressed Steel Company, Ltd., in memory of its late managing director. At the same time an appeal to metallurgical industry organized by the late Major A. Pam gave part of the money needed to set up metallurgy as an independent subject in the University, and the remainder was generously provided by the University Grants Committee. At the moment, the Department of Metallurgy exists as an independent department in rooms in the Old Physiology Building. A new laboratory has been designed as part of the Keble Triangle scheme, and the building of this is to begin before the end of this year.

In June 1956 the University established a new Honour School in the Science of Metals, and students are now being accepted for this. The creation of the Wolfson chair of metallurgy thus means that the subject is properly established in the University, with permanently endowed professorship and readership, and a modern laboratory the building of which is about to begin. In view of the shortage of metallurgists in Great Britain, this expansion of metallurgical facilities at Oxford is much to be welcomed.

Metallurgical industry is one of the oldest of the arts but one of the youngest of the sciences. Whereas in chemical industry many processes are the earlier laboratory experiments done on a large scale, metallurgical industry has developed mainly from the older arts and crafts. It is only in comparatively recent times that any considerable fundamental work has been carried out on metals and alloys. The progress made since the First World War has been enormous, and there are now well-established and rapidly growing branches of science which are related to metallurgical industry in the same way that the science of chemistry is related to chemical industry.

The intention of the Oxford honour course in the science of metals is to combine a training in the science of chemistry with a knowledge of the fundamental science of metals and alloys. Technology as such is not taught, although much of the work in the science of metals course is related to industrial processes.

The new honour course involves four years of study, and is combined with part of the existing Honour Chemistry course. In the first three years the student reads the full Oxford course in inorganic and physical chemistry, but organic chemistry is dropped at the end of the first year, and is replaced

by the science of metals. At the end of the third year, the student takes Part I of the Final Honour Examination, which consists of the normal written papers and practical examinations in inorganic and physical chemistry, together with written papers and practical examinations in the science of metals. The passing of this examination enables the student to take the B.A. degree, but to obtain classified honours a fourth year must be spent at research work on an approved metallurgical subject.

The four-years course outlined above should be of high scientific value. It brings the student into contact with all three branches of chemistry, two of which are studied to an advanced level, together with some branches of physics and of the newer sciences of the solid state. It is also directly related to the industrial practices of metallurgy. The inorganic chemistry should enable the graduate to understand the principles underlying the extraction and smelting of metals. The physical chemistry should make him familiar with the principles of chemical equilibrium and reaction kinetics, and so enable him to understand processes such as slag/metal equilibria, fuel/gas reactions, etc. Finally, the metal-science part of the course should teach the student much about the structure and properties of metals and alloys, and their relation to processes involved in industrial practice. It is hoped that a graduate trained on these lines will be a useful man (or woman) in many ways. If he enters industry, he will, of course, have to learn the technology of his subject. This is the case with graduates in physics or chemistry whose university training is in pure science, and it is hoped that metallurgical industry will find many uses for men trained in the sciences of chemistry and of metals.

The Department of Metallurgy at Oxford also offers facilities for postgraduate research work for the B.Sc. and D.Phil. degrees. The laboratory is well equipped for thermal analysis, microscopical metallography, X-ray metallography, and electron microscopy. The staff at present consists of one reader, Dr. W. Hume-Rothery, two lecturers, Dr. J. W. Christian and Dr. J. W. Martin, and one graduate assistant, Dr. A. Hellawell.

OBITUARIES

Prof. Frank Horton, F.R.S.

Prof. Frank Horton, emeritus professor of physics in the University of London, died on October 31, at his home in Cambridge. He was the eldest son of Albert Horton, of Olton, Warwickshire, and was born on August 20, 1878; his mother's maiden name was Kate Louisa Carley.

Horton began his academic career at King Edward VI Grammar School, Birmingham, and even at that early date began to devise and carry out experiments in physics. Leaving school, he proceeded to Mason College (later the University of), Birmingham. Here he obtained first-class honours degrees in both physics and chemistry, and then began a series of researches on the elastic properties of wires and quartz. In this work, directed by Prof. Poynting, use was made of a variation of the 'method of coincidences' for determining a periodic time. An account of this work appeared in the *Philosophical Transactions of the Royal Society* and earned for Horton his first doctorate at the University of London in 1903.

In 1901 Horton went to St. John's College, Cambridge, as an 1851 Exhibition Research Scholar. For his research work with Sir J. J. Thomson, during which Horton became interested in the production of high vacua, he was elected a Mackinnon Research Student of the Royal Society in 1903. Among their other activities, Thomson and Horton found time to edit the important series of Physics Monographs, published by Longmans, Green and Co., Ltd. In 1905 Horton was made a Fellow of St. John's and during 1905–13 was a lecturer at the Cavendish Laboratory.

At the age of thirty-five, Horton was elected to the chair of physics at the Royal Holloway College, Englefield Green, Surrey. The earlier occupants of this chair were Prof. H. L. Callendar, Prof. W. Cassie and Prof. P. V. Bevan. Prof. Horton's work at Cambridge had equipped him with the tools necessary to carry on fundamental work on electronics and soft X-rays. During the First World War he investigated, among other things, the effect of helium on the stability of electron emission from heated filaments.

In 1911 Frank Horton married Miss Vera Fulton, of New Zealand, where the marriage ceremony took place, and his daughter, Ngaire, now Mrs. Bajko, survives him. She lives in New Zealand and has a son, Michael.

In 1923 Prof. Horton was elected a Fellow of the Royal Society and two years later, as a member of the Senate of the University of London, found himself in the thick of many controversies then current in academic circles; he was always a champion of the rights of university teachers. As chairman of many university bodies he was meticulous in the dispatch of business. He was dean of the Faculty of Science during 1930–34 and in 1932 was elected a member of the Court of the University. In September 1939 he became vice-chancellor, a post which he held until 1945—such was the measure of the confidence his colleagues had in him as an administrator of the highest order. Earlier in 1939 he married one of his former students and a co-research worker, Miss Ann Catherine Davies, who was staff lecturer in physics at the Royal Holloway College during 1922–29, when she left to take up a post at Newnham College, Cambridge, where she is now vice-principal. Mrs. Horton is an active member of the Council of Royal Holloway College, and this enabled Prof. Horton to keep in contact with the scene of his former labours when he retired in 1946 from his chair of physics and went to live in Cambridge.

His successor, Prof. S. Tolansky, found the laboratories in the department which Horton had helped to design in the middle 'twenties well equipped to meet the needs of present-day workers in physics. These laboratories form part of a block which houses both the Botany and Physics Departments of the College, and when they were opened in 1928, Prof. Horton paid high tribute to Dr. Margaret Benson, head of the Botany Department during 1893–1922 (she occupied the chair during 1912–22), for it was

she who had conceived the idea for the erection of a new building and had done so much to bring it to fruition.

Horton was a physicist gifted with remarkable experimental skill, and those who worked with him were inspired by the dextrous and confident manner in which he would handle and adjust highly sensitive instruments. He was never more pleased than when he could watch an undergraduate carrying out an experiment with meticulous care.

The funeral service was held on November 2 at St. John's College Chapel, and the large attendance on that occasion testified to the high esteem in which Prof. Frank Horton was held. C. J. SMITH

Dr. Paul D. Merica

WE regret to announce the death of Dr. Paul D. Merica, of the International Nickel Co. of Canada, in New York on October 20. Dr. Merica was born in Warsaw, Indiana, in 1889. He attended De Pauw University during 1904–7, graduated from the University of Wisconsin in the following year, and received his Ph.D. from the University of Berlin in 1914. During 1914–19 he was associated with the metallurgical division of the U.S. Bureau of Standards in Washington. Dr. Merica carried out a number of researches on duralumin and other aluminium alloys and developed his theory of the precipitation hardening of metals and alloys.

Dr. Merica first became associated with the International Nickel Co. in 1919, becoming director of research and later assistant manager of the Development and Research Department. He was made president of the company in May 1952, retiring from the last post in April 1954.

For his contribution in the field of metallurgy and outstanding leadership in physical metallurgy, Dr. Merica, who was a member of the U.S. National Academy of Sciences, was awarded the James Douglas Medal in 1929, the John Fritz Medal in 1938, the Institute of Metals Medal in 1941, the Franklin Institute Medal in 1942, and American Society for Metals Gold Medal in 1951. Dr. Merica was an honorary member of the American Institute of Mining and Metallurgical Engineers, of which he was a former vice-president and director, as well as of the American Society for Metals.

NEWS and VIEWS

Metallurgy at Oxford: Prof. W. Hume-Rothery, O.B.E., F.R.S.

THE development of metallurgical science at Oxford has been continuously associated with the work of Dr. Hume-Rothery, and his many friends will warmly welcome his appointment as the first Isaac Wolfson professor of metallurgy (see p. 1319 of this issue). Dr. Hume-Rothery was at the beginning of an army career when a serious illness left him totally deaf. Despite this affliction, he obtained a first in chemistry at Oxford and a Ph.D. at the Imperial College of Science and Technology, London, before returning to Oxford to found the research school in alloy theory, which soon became internationally famous. He was elected a Fellow of the Royal Society in 1937, and he was Warren Research Fellow of the Society during 1932–55, when he became the first holder of the George Kelley readership. Post-war developments in the teaching of metallurgy are largely the result of his enthusiasm and hard work. Dr. Hume-Rothery's early experimental work led to our present understanding of many of the factors governing the form of metallurgical equilibrium diagrams. Perhaps the best-known results are the discovery of the 'electron compounds' and the enunciation of the famous size-factor rule. During the War, his group worked on complex aluminium alloys, and since then his main interest has been in high melting point alloys of the transition metals. He is equally distinguished as the author of five text-books, and his very successful expositions of modern theories have been translated into many languages. Dr. Hume-Rothery was awarded the platinum medal of the Institute of Metals in 1949, and has also received awards from scientific societies in the United States, the Netherlands and Italy.

Reports of the Nationalized Industries in Britain

IN a debate in the House of Commons on November 26, which took note of the annual reports and statements of accounts of the Gas and Electricity Industries, the Paymaster-General, Mr. R. Maudling, as representing the Minister of Power, said that the surplus of £3·8 million shown in the latest report of the gas industry is due to the increased efficiency of the industry. The number of units in the industry have been reduced from 1,050 at vesting day to 611; the thermal efficiency has been increased to 77·8 per cent, and although the cost of coal and manual labour has risen by 65 per cent since 1950, the price of gas, which represents two-thirds of the industry's sales, has risen by only 47 per cent, and that of coke and by-products by 78 per cent. Mr. Maudling referred to the increasing competition of electricity and the increasing scarcity and cost of good-quality coking coal. The industry is accordingly seeking to exploit lower-grade cheaper coal, and much work is being done on the Lurgi process of complete gasification and on the hydrogenation of oil and coal. The Lurgi process, however, yields gas of low calorific value, and it has not yet been fully proved with grades of coal available in Britain; but if the work of the North Western Board on hydrogenation is successful, it should be possible to produce gas of good quality from a wide range of comparatively low-quality, low-priced coal. Both the Lurgi process and hydrogenation have the advantage of producing no coke, of which there is at present a surplus. The industry is also examining the use of surplus products from the oil refineries, as well as of imported oil, and, besides prospecting for natural gas in Britain, is studying the import of liquefied methane, the use of coke-oven gas and, in co-operation with the National Coal Board, the use of methane from coal pits, as well as both the long-distance transmission and the storage of gas.

Turning to the electricity industry, Mr. Maudling said that total sales last year increased by 6·7 per cent, and sales to farms by 18 per cent, while the average price of electricity sold by the Central Electricity Board increased by 4·7 per cent. Since 1948 the

cost of fuel has risen by 55 per cent, but the price per unit has risen by only 26 per cent. It is expected that the reduction in oil-firing will result in an increase in the consumption of coal by about 2·5–3 million tons a year in the 1960's. Mr. Maudling did not think that there should then be an embarrassing surplus of small coal, but other uses of small coal are being investigated. As regards capital investment, the present rising level of investment in electricity will continue but at a lower rate than previously planned. In the nuclear power programme, the development of Bradwell, Berkeley, Hinckley Point and Hunterston will proceed as planned, but there will be some delay in starting the later stations in the programme and the net effect will be to delay the completion of the full programme by one year. In repeating the assurances previously given in the White Paper and elsewhere that the accident at Windscale could not occur in the power stations being built for the Central Electricity Authority, Mr. Maudling emphasized that this applies equally to the power stations which the industry is offering for sale abroad. He added that a reactor safety committee has been established on which Lloyd's and the British insurance industry are represented, and a formal safety code for the design and operation of nuclear power stations is being prepared. As regards the siting of nuclear power stations, Mr. Maudling argued that there is neither the time nor the trained staff for a complete survey of the United Kingdom before decisions are taken, but he did not meet the objection that such a survey is only demanded when ti is proposed to invade national parks or like areas.

Brussels Universal and International Exhibition, 1958

Work on the 500-acre site for the Brussels Universal Exhibition continues apace, and the majority of the structures are ahead of schedule. Most of the buildings have taken their final shape, and work is now in progress on interiors and exhibits. About 8,000 men are at present working on the site. Two of the nine spheres of the 'Atomium' have been completed, and three others have their main structure in position. Work has begun on the topmost sphere, and the lift mechanism has been installed in the central column.

Details are also available of some of the plans for the International Hall of Science, sponsored by fifteen nations. All the exhibits are to be of a collective and non-national character. The hall will have four sections: The Atom; The Crystal; The Molecule; The Living Cell. The Atom Section will include displays of radioactive elements, nuclear and thermonuclear reactions and solar energy. There will be models of accelerators from the European Nuclear Energy Centre at Geneva, a demonstration of the direct use of solar energy in a furnace, and a fully operating experimental reactor. The Crystal Section will contain, among other things, a model of a crystal 13 ft. × 13 ft., containing 800 lights showing the basic elements of the crystal. The Molecule Section will explain analytical, synthetic and physical chemistry. Its main feature will be a model of a crystallized virus. The Living Cell Section will allow the public to see, by means of a prototype colour-television set, essential cell activities otherwise only visible by microscope. There will also be illustrations dealing with chromosomes, heredity, blood groups, cell division, and photosynthesis.

Nordic Institute for Theoretical Atomic Physics

The five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) have set up a joint organization, under the chairmanship of Prof. Niels Bohr, for the purpose of strengthening scientific co-operation in the field of atomic physics. One of the main objects of the organization is the establishment of the Nordisk Institut for Teoretisk Atomfysik in Copenhagen in a building which will be erected by the Danish Government in connexion with the existing premises of the Institute for Theoretical Physics of the University of Copenhagen. Further activities envisaged are exchange of Nordic scientists, organization of symposia, and visits of scientists from other countries to Nordic physics institutions.

Research work and educational activities will be the task of the staff of the Nordic Institute. Facilities will be provided for a number of younger physicists from the member States to receive advanced training in the field of theoretical atomic physics. For the interim period, until a formal agreement has been established by the participating governments, C. Møller has been appointed director of the Institute (during his absence on a visit to the United States, T. Gustafson is acting as director), assisted by G. Källén, B. Mottelson and S. Rozental. On February 1, L. Rosenfeld will join the permanent staff of the Institute.

Journal of Mental Deficiency Research

The causation of mental disease of all types has tended to attract research workers perhaps less than in any other branch of medicine, and only the truly devoted have turned their energies into trying to discover the causes of mental deficiency. At first sight the mental defective seems so hopeless, so finally damaged, that one feels despair. Nevertheless, research is worth while, and the realization that certain of the acute specific fevers can injure the fœtus has aroused new hope. Those who work on these problems tend to be scattered in mental deficiency hospitals and work a great deal isolated from others engaged in similar activities. It is an excellent thing, and one which will be most welcome, to find that a journal has been founded to record their researches (*Journal of Mental Deficiency Research*, **1**, No. 1 (July 1957). Pp. 65. Published half-yearly. Annual subscription rate: 15*s*. Single issues 7*s*. 6*d*. or 1.50 dollars. Publishing manager: Mr. A. Highfield, 10 Shendon Way, Sevenoaks; 1957). The first number contains an excellent article by Penfield on "The Genetics of Anencephaly", a paper by Claridge and O'Connor on "The Relationship between Incentive, Personality Type and Improvement in Performance of Imbeciles" and "A Survey of Mental Deficiency Types in the United States of America". A paper is contributed by Mittwoch on "Some Observations on the Leucocytes in Mongolism", and there is another article on phenylketonuria by Hsia, Paine and Driscoll. It is hoped that this valuable journal will have a long life and will be able to maintain the high standard of its initial number. It is essential to all who are interested in mental deficiency and will be consulted by anyone who hopes to further research.

Annales de l'Institut Phytopathologique Benaki

There is nothing in the first number of a new series of the *Annales de l'Institut Phytopathologique Benaki* (Nouvelle Série, **1**, No. 1, 1957. Pp. 90. Kifissia-Athenes: Institut Phytopathologique Benaki,

1957), which is well produced, with large print and generous margins, to show whether it is typical of what is to come. Its ninety pages consist solely of a thesis presented for a doctorate by D. G. Zachos to L'École de Hautes Études Agronomiques d'Athènes. The work described was done at the Station Centrale de Pathologie Végétale, Versailles, and falls into three parts: the first deals with the movement of tobacco mosaic and potato *X*-viruses in tomato plants, the second with interactions between the two viruses which together cause streak of tomatoes, and the third with the effects of infection on certain oxidizing systems. The most striking phenomenon reported is that, in plants simultaneously infected with tobacco mosaic virus, potato virus *X* may reach more than three times the concentration it reaches in plants infected with it alone, but considerable evidence is also presented indicating a correlation between virus multiplication and the activity of three oxidases, with catalase activity varying inversely with that of the oxidases.

Microrecording in Libraries

THE Library Association has recently published as Pamphlet No. 17, entitled "Microrecording in Libraries", by J. Burkett (Pp. 55. London: Library Association, 1957. 8*s*. 6*d*.), a review of present practice which provides a most useful and concise account of the various types of microrecord and ancillary apparatus with a discussion of their advantages as well as their limitations. Publishing facilities are summarized and there is a section on uses of microphotography, including a note on the use of microrecording in university and other libraries in Britain. Guidance is given on the choice of both process and reader, and there is a good bibliography. Although the pamphlet is well up to date, it just misses including a reference to the new and greatly improved portable microfilm and microfiche 'Dagner' reader, developed by J. H. Mullens of The Hague, which on price grounds alone has special claims on the interest of the university or technical college libraries.

Research Guide

"Scientific Research in British Universities, 1956–57" (pp. vii +405. London: H.M. Stationery Office, 1957. 22*s*. 6*d*.), like the previous volumes in this series, provides brief notes on scientific research in progress in British universities and university colleges during the period in question, describing the nature of the projects in sufficient detail to indicate the scope of the research. Under each entry the departmental head is named, together with those of members of the staff engaged in supervising research, and the entries are arranged alphabetically, first by universities and university colleges and then by subject. There are alphabetical name and subject indexes. The material has been collected by the British Council from heads of university departments.

Science in the Primary School

A USEFUL introduction to science has been described by B. L. H. Hampson, of Thomas Street School, West Gorton, Manchester (*School Nature Study*, **52**; October 1957). He suggests that science teaching in the primary schools should no longer be restricted to Nature study, and that there should be substituted instead a logical starting-point for a general science training and the establishment by progressive stages of a comprehensive foundation of general science knowledge from which any secondary phase of science education could be developed. Ways in which these principles have been put into practice in his own school are described as well as the conclusions reached by Hampson after six years experience. Recent reports have shown that the principles enunciated have been applied in both junior and infant schools in other parts of Britain.

Further Education in the North of England

THE tenth annual report of the Northern Advisory Council for Further Education contains interesting information about the way the pattern of technical education in the north of England has changed recently. Between 1954–55 and 1956–57 the number of full-time students increased from 3,797 to 4,640; part-time day students increased from 21,882 to 26,482. In evening classes at technical colleges, however, the increase in the number of students was very slight, from 27,179 to 29,179; in evening institutes the number of students decreased from 75,328 to 62,680. These changes were reflected in the kind of courses for which students enrolled. The number of students taking the more advanced studies—degree, higher national, diploma, college diploma, or higher national certificate—increased from 2,403 in 1954–55 to 3,040 in 1956–57. The report may be obtained from the Secretary, 5 Grosvenor Villas, Newcastle upon Tyne.

Transistors

EXTENSIVE research and development work on semiconductors, in particular on transistors and related devices, and on their applications, has recently been carried out within the Radio Corporation of America, which has agreed to publish a selection of papers describing the work as it applies to the theory, fabrication and application of transistors. The first volume has now been issued (Transistors I: R.C.A. Laboratories. Second printing, 1957). It consists of published and unpublished papers and abstracts. Two review articles deal with basic transistor device concepts and new advances in the junction transistor. In other papers the concepts are further extended and applied to new and improved devices. For example, the limitations of diffusion phenomena on the frequency response of transistors, and the drift transistor.

Lighting, Heating and Ventilation of Museums

In the *Museums Journal* of October, Messrs. W. E. Rawson-Bottom and B. S. Cooper contribute an important paper on the use of both natural and artificial lighting in museums. Following a brief review of early attempts in lighting, its present value as one of the essential factors of effective display is stressed. The first author deals with general lighting in the museum and favours the standard fluorescent batten unit for one or two lamps with louvres in short lengths of moulded plastic material which clip to the lamps. He also feels that the incandescent lamp is still useful in many places; for example, geological specimens and jewels tend to lose brilliance and gold can look like brass in fluorescent lighting. He then deals with the lighting to be adopted with various types of museum cases: in art gallery lighting he advocates fluorescent lighting in trough reflectors with 75-watt tungsten lamps for colour correction. The second author is concerned with the effects of photochemical deterioration and

concludes that the removal of ultra-violet radiation by means of suitable filters, while in some instances an advantage, usually leads to only an insignificant increase in the photochemical stability of the illuminated material.

In the same issue of the *Museums Journal*, another paper, on the heating and ventilation of museums, by Dr. A. E. A. Werner, Research Laboratory at the British Museum, discusses a complex subject previously viewed in a rather empirical way. The author outlines the basic principles concerned in determining a reasonable atmospheric environment in museums and considers the practical problems involved in air-conditioning, and the various types of apparatus employed both for exhibition and storage areas. The three essentials—humidity, temperature and air movement—are considered and reasonable limits are defined. The paper is illustrated by graphs, diagrams and photographs of apparatus.

Museum of Applied Arts and Sciences, Sydney

The annual report for 1956 of the Museum of Applied Arts and Sciences at Sydney is a purely factual statement concerning a year of progress of this well-known institution. Such is the popularity of the planetarium that serious consideration is being given to the replacement of the present projector and dome with a larger unit accommodating at least a hundred people. The chief exhibit acquired in 1956 consists of five dioramas and a flow chart presented by the Petroleum Information Bureau (Australia). The dioramas illustrate the origin of oil, exploration of potential areas, drilling processes, recovery of oil from wells, transport to refinery and uses of oil in the home. The flow chart depicts the refining of crude oil by fractional distillation. The reputation of this Museum for scientific research, especially in the field of the botany and chemistry of the essential oil-bearing flora of Australia, is being pursued, and many papers have been published.

Solar Energy and the Depth of the Earth

Since 1946 N. V. Belov and V. I. Lebedev have published a number of articles in which they have developed their hypothesis of the probable source of energy of endogenetic processes, and now they have presented their final and comprehensive outline of this hypothesis (Belov, N. V., and Lebedev, V. I. *Priroda*, No. 5, 11; 1957). It is based mainly on a characteristic fact in leptology (crystal chemistry), namely, that in the minerals occurring in superficial sedimentary rocks, such as the clays, aluminium is surrounded by six oxygen atoms in octahedral co-ordination, with the Al–O distances of the order of 1·9 A., while in the minerals of the deep-seated igneous and metamorphic rocks, such as the felds-pars, aluminium is surrounded by four oxygen atoms in a tetrahedral co-ordination, with the Al–O distance of the order of 1·7 A. The contraction of this distance during the downward movement of the Earth's crust is, according to the authors, an important source (the effect of radioactive disintegration not overlooked) of energy which produces the rise of temperature in depth, and is consequently responsible for the processes of metamorphism and magmation. Thus, aluminium and oxygen, as well as other cations, are acting as accumulators of solar energy, the charging of this 'geochemical accumulator' taking place in the zone of weathering, and its discharge in the depth of the Earth's crust. Similar conclusions have been reached by V. A. Saul (*Geochim. et Cosmochim. Acta*, **8**, 86; 1955) entirely on the basis of the data of thermochemistry.

International Union of Pure and Applied Physics

At the ninth General Assembly of the International Union of Pure and Applied Physics held in Rome during September 17–20 the U.S.S.R., Austria and Bulgaria were formally admitted to the Union. The number of countries now adhering to the Union is thirty. For the period 1957–60 the Executive Committee of the Union has the following members: *President*, E. Amaldi (Rome); *Former Presidents*, N. F. Mott (Cambridge), M. Siegbahn (Stockholm); *Vice-Presidents*, J. de Boer (Amsterdam), R. B. Brode (Berkeley), M. Kotani (Tokyo), J. H. Van Vleck (Cambridge, Mass.), G. Herzberg (Ottawa), A. Joffe (Leningrad), E. Rasmussen (Copenhagen), H. Staub (Zurich), F. C. A. Trendelenburg (Erlangen), J. Weyssenhoff (Cracow); *Secretary General*, P. Fleury (Paris).

Eight specialized Commissions were authorized to develop international co-operation in the following fields (names of presidents and secretaries are indicated in brackets, with the addresses of the secretaries): Symbols, units and nomenclature (H. H. Nielsen, Columbus, Ohio; J. de Boer, Finsenstraat 28, Amsterdam, Netherlands); thermodynamics and statistical mechanics (J. Yvon, Paris; G. Careri, Universita degli Studi, Rome); cosmic rays (B. Rossi, Cambridge, Mass.; C. F. Powell, H. H. Wills Physical Laboratory, Royal Fort, Bristol 8); very low temperatures (C. J. Gorter, Leyden; D. Shoenberg, Cavendish Laboratory, Cambridge); publications (J. H. Awbery, London; G. A. Boutry, 292 rue Saint-Martin, Paris 3°); acoustics (W. Furrer, Berne; C. W. Kosten, Mijnbouwplein 11, Delft, Netherlands); solid state physics (this commission is composed of three sub-groups): general study (J. C. Slater, Cambridge, Mass.; C. Kittel, Department of Physics, University of California, Berkeley 4, California); semiconductors (A. Joffe, Leningrad; R. A. Smith, Royal Radar Establishment, Malvern); magnetism (L. Néel, Grenoble; L. F. Bates, Department of Physics, University of Nottingham); high-energy physics (C. J. Bakker, CERN, Geneva; R. E. Marshak, University of Rochester, U.S.A.).

International Collegium for Neuro-Psycho-Pharmacology

A meeting was held in Zurich on September 3 during the Second International Congress for Psychiatry of investigators from different countries for the purpose of founding an International Collegium for Neuro-Psycho-Pharmacology. It was decided unanimously that such a Collegium should be formed with the objects of promoting research and the exchange of ideas, as well as collaboration in the fields of experimental and clinical neuro-psycho-pharmacology. It is proposed to organize special symposia as well as general meetings. Prof. E. Rothlin (Switzerland) was elected president, and Profs. Trabucchi (Italy), Hoch (United States), Delay (France), Delgado (Peru), Hoff (Austria) and Dr. Shepherd (United Kingdom) as vice-presidents. It is hoped that it will be possible to hold the first international meeting of the Collegium in 1958, and an executive committee, consisting of

Profs. Rothlin and Trabucchi, together with Drs. Deniker (France), Denber (United States), Bradley (United Kingdom) and Radouco-Thomas (Switzerland), was appointed to make the necessary arrangements.

Canadian Federation of Biological Societies

THE Canadian Federation of Biological Societies was instituted in Ottawa on October 11. The Federation comprises four member societies: the Canadian Physiological Society, the Pharmacological Society of Canada, the Canadian Association of Anatomists and the Canadian Biochemical Society. The Canadian Physiological Society has been active since 1935. The other three societies have been founded in the past two years; many of their members already belong to the Canadian Physiological Society. However, the rapid growth of these sciences has made it desirable to form societies for the individual disciplines not only to further their development in Canada but also to meet international obligations. The purposes of the Federation are to bring together persons who are interested in teaching and research in the biological sciences, to disseminate information on the results of biological research through scientific meetings and through publication, to encourage exchange of information between constituent societies, and to act for the member societies when it is agreed that concerted action is desirable. At the invitation of Queen's University, the Canadian Federation of Biological Societies will hold its first annual meeting in Kingston, Ontario, in June 1958.

Meteorites Conference in Moscow

A BRIEF report on the seventh Meteorite Conference, which was held in Moscow towards the end of 1956, is published by E. L. Krinov (*Priroda*, No. 7, 57; 1957). The Conference was attended by about a hundred delegates, and thirty papers were read and discussed. A number of papers dealt with the calculation of the orbits of meteorites, which in all cases proved to be elliptical; this suggests that meteorites are derived from bodies belonging to the solar system, most probably asteroids. On the basis of a large number of chemical analyses of meteorites, A. A. Yavnel has concluded that these may be referred to five distinct groups, each group probably corresponding to a parent asteroid. Other topics discussed included meteorite dust, isotopes in meteorites and age of meteorites. A full report will appear in the journal *Meteoritica*.

Harwell Reactor School

THE Reactor School at Harwell is to increase the number of courses to be held each year. Four standard courses will be held instead of three, each lasting sixteen weeks (beginning in January, April, September and October), and there will also be two courses for senior technical executives, each lasting nine days (in May and September). Further details can be obtained from the Principal, Reactor School, Atomic Energy Research Establishment, Harwell, Didcot, Berkshire. Applications must be submitted three months before each course begins; the January course has already been filled.

Scholarships Abroad

MORE than one hundred scholarships are being offered to British students by nineteen foreign countries for study abroad during the academic year 1958–59. The countries offering the scholarships are: Austria, Belgium, Brazil, Denmark, Finland, France, Germany, Iceland, Iran, Italy, Japan, The Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland and Yugoslavia. Most of the scholarships correspond to awards made by the British Council to students from these countries for study in the United Kingdom. The British Council assists in publicizing the offers and in most cases in the recruitment of candidates. Closing dates for applications vary according to the country concerned, the earliest being February 1, 1958. Further information and application forms, for which a stamped addressed foolscap envelope should be sent, can be obtained from any British Council office, or from the Director, Universities Department, British Council, 65 Davies Street, London, W.1.

Announcements

THE Order of Merit has been conferred on Lord Waverley, chairman of the Port of London Authority, formerly Lord President of the Council (as Sir John Anderson).

DR. H. G. KUHN, reader in physics, University of Oxford, has been awarded a Cherwell Fellowship by the William Waldorf Astor Foundation of New York to enable him to work for a few months at the University of California, Berkeley.

THE annual conference of the Geographical Association will be held at the London School of Economics, Houghton Street, London, W.C.2, during December 31–January 3. Further information can be obtained from R. C. Honeybone, University of London Institute of Education, Malet Street, London, W.C.1.

THE Radio Industry Council offers six premiums of 25 guineas each, for articles on electronics published in 1957, to any writer not earning his living wholly or mainly by writing. Articles for consideration should be sent to the Secretary of the Radio Industry Council, 59 Russell Square, London, W.C.1, before the end of the year. Six copies, with a signed declaration of the eligibility of the writer or writers, should be submitted.

A POST-DOCTORATE fellowship, to commence in the summer of 1958, is available in the Physics Department at Dalhousie University. The fields of research under investigation are acoustics, high-frequency gas discharges, nuclear physics, solid-state physics and theoretical physics. Further information can be obtained from the Physics Department, Dalhousie University, Halifax, Nova Scotia, Canada.

ERRATA. In the communication entitled "Triphosphopyridine Nucleotide as a Catalyst for Photosynthetic Phosphorylation" in *Nature* of July 27, p. 182, the following corrections are necessary: (1) p. 183, col. 1, line 2, after "vitamin K" insert "(a high concentration of either riboflavin phosphate or vitamin K masks the requirement for triphosphopyridine nucleotide; details will be presented elsewhere)"; col. 2, last sentence in the middle paragraph should read "The reduction of triphosphopyridine nucleotide was not specific; diphosphopyridine nucleotide was also reduced, but in our case at a lower rate (compare ref. 12)"; Table 2, third column units for "(μmoles)" read "(μatoms)".

QUALITY CONTROL IN FOODS

A JOINT meeting of the Association of Public Analysts and the Food Group of the Society of Chemical Industry was held in London during October 3–4 to discuss quality control of food.

The term 'quality control' was intentionally given a very wide interpretation and a diversity of points of view and experience were expressed, including those of the manufacturer, the consumer, and the analyst.

There were three papers concerned primarily with statistics. Dr. E. C. Wood started the series with a relatively simple explanation of the basic concepts, explained many of the terms likely to be used during the symposium, and illustrated simple applications of statistical methods to experimental results. A later paper by Dr. E. H. Steiner went more deeply into the three main sources of error, those due to analysis, sampling and natural variation, and the separation of errors by the analysis of variance. This included valuable advice on sampling procedures appropriate to situations either where the acceptable degree of risk has been predetermined or where there is no previous knowledge of the variation expected.

Mr. J. H. Harries spoke on the validity of organoleptic tests as a means of quality control. He stressed the importance of putting the right kind of question to taste panels, and illustrated his points by reference to a number of score sheets of individual design for the analytical comparison of the qualities of various foods. He directed attention to the possibility of applying multivariate analysis to an examination of the step values in arbitrary scales, and also referred to techniques for avoiding numerical intervals without losing the advantages of statistical interpretation of the data obtained.

A paper on the practical application of statistics to the bacteriological control of canned meats, by Dr. H. Riemann, of the Danish Meat Research Institute at Roskilde, was read by his colleague, Mrs. E. Blomquist, who later gave a paper of her own on another practical example of statistical quality control in the production of luncheon meat. The former directed attention to the relation between batch size, the number of samples tested and the degree of confidence with which it could be assumed that the samples gave an accurate measure of the bacterial quality of the batch. It was pointed out that the sampling methods discussed might give a good picture of general quality, but to safeguard against the occurrence of such dangerous organisms as *Clostridium botulinum*, the number of samples necessary might be unpractical. A most careful watch on raw materials and ingredients and efficient supervision of processes were necessary. The example described in Mrs. Blomquist's paper, although mainly concerned with the mathematics of variations in tare and net weight of cans and the operation of quality control charts, also dealt with some of the practical details, and indicated that such methods are worth while if the findings are used appropriately by the management, and can then be of considerable financial benefit.

Six of the papers were given by technologists from different branches of the food industry. Dr. A. G. Lipscomb described the practical application of quality control methods in the chocolate and confectionery industry. It is necessary to ensure that raw materials conformed to specification in composition and were of the expected flavour; proportioning and processing must be kept within budget limits; the product must reach the standard expected by the consumer and have an adequate shelf-life without loss of appearance or flavour. Physical assessments such as determinations of fat or the particle size in chocolate lend themselves to statistical treatment and to the use of quality charts as a means of judging performance. Comparisons of means and deviations could be utilized to diagnose errors in machine settings. Subjective assessment of raw materials and finished products is essential. Practical advice on experiment design and the management of taste panels was given. The intersection of the curves of cost of production and sale price when plotted against quality show only a restricted area of profitable operation, so quality control alone does not ensure dividends.

Dr. W. B. Adam said that fruit and vegetable canners made only limited use of statistical methods in routine control, but nevertheless such methods had been valuable for specific investigations. He referred particularly to the variability of can weights and filled weights, and the difference between the original weight of fruit in a can and the subsequent drained weight. Subjective assessment, allied to suitably designed score cards, is of great assistance in recording the quality of canned fruit or vegetables, but experienced buyers rely on mental integration of their observations rather than on mathematical calculations. Mechanical aids such as the tenderometer used for forecasting the optimum maturity of a pea crop were briefly described and explained.

Dr. R. J. MacWalter spoke on quality control in milk and dairy products. The relations between producer and buyer of milk are somewhat unusual, since apart from the brief judgment of an expert nose the quality of milk is probably not known until after it has been accepted, bulked, pasteurized and passed on. Nevertheless, a number of tests are applied to samples before distribution to ensure conformity with legal requirements, efficiency of heat treatment, freedom from contamination and control of measure in bottle. Reference was made to the problems of sampling evaporated or sterilized milk products in order to reach an adequate degree of assurance that the product is safe and the spoilage rate minimized. Grading methods for cheese and butter were mentioned. A graphic illustration was given of the relationship between bacterial contamination counts and standards of factory hygiene in rival creameries.

Quality control of open packed meat products was discussed by Mr. S. Brightwell. Variability in availability of raw material complicates the maintenance of uniform quality in sausages. Several sensory qualities by which they are judged—such as juiciness, texture and flavour—are not easily assessed numerically or given definite weighting. It is important to trace the causes of reported variations in quality. It was noted that tasters' views on saltiness do not necessarily agree with chemical analyses, and a seasonal variation in the sensitivity of panels to saltiness was mentioned. A sensory assessment by an expert might be accepted in preference to a laboratory report where these were in conflict.

It is difficult to measure dough so accurately that after baking all loaves or all biscuits will fall within a narrow weight-range. Dr. R. Falconer described how control charts could profitably be used to give warning that re-adjustment of machines was desirable, and spoke of the possibility of extending the application of appropriate methods to other observations necessary for good management in the baking industry.

The fish industry depends in no small measure on the Department of Scientific and Industrial Research for technical guidance. Industry has felt a need for better methods of control of quality, and practical help has been given by introducing well-organized subjective assessments and by compiling scientific data. Dr. C. L. Cutting mentioned in particular a system of grading kippers which the industry has welcomed and which may lead to improved quality. The occurrence of parasitic worms in fish from certain fishing grounds has been studied statistically and constructive recommendations formulated.

An interesting paper from quite a different aspect of the subject was given by Dr. R. A. Scott on the automatic control of proportioning and mixing. He gave details of practical methods of measuring liquids and powders, and of various types of automatic weighing and delivery devices, culminating in explanatory diagrams of fully automatic plant for weighing, delivering and mixing six or more ingredients according to formulæ fed to a control panel on a punched card. In such systems there are devices designed to eliminate as many as possible of the known causes of undesirable variation.

The factory manager's outlook on quality control was indicated by Mr. M. Bogod. Such control is welcome where it is an aid to economical production, improved service to customers or conformity with legal obligations. So far as possible, interference with the flow of production should be avoided. Sometimes the nature of the control can be designed so that automatic adjustments can be made to correct undesirable trends. Great importance is attached to cordial co-operation from operational and supervisory staff. This can be achieved only where they understand how quality control can improve matters. The spot judgment of expert individuals is usually preferable to that of taste panels in detecting deviations from the normal in flavour or appearance.

Public analysts exercise quite a different form of quality control. Mr. E. G. Whittle expressed their point of view. They are concerned first with compliance with legal requirements, and secondly that foods conform to what the customer is led to expect. It is often difficult to decide desirable limits of variation of quality in foods, but the Association of Public Analysts has a part in helping the Foods Standards Committee to reach conclusions on these matters. Statistics have been valuable to analysts in agreeing on the natural limits for the freezing point of milk and to a lesser extent in accounting for the effects of natural variation in raw materials used in food such as jams. The work of a magistrate's court would not, however, be made easier if a public analyst expressed his findings in terms of statistical probabilities.

Mr. D. H. Pickard brought to the symposium his views on quality as a market research worker. He pointed out that the consumer in his judgment of quality uses very different criteria from those of the manufacturer or public analyst. They are influenced not only by the inherent qualities of a food product but also by imputed qualities. Appearance, for example, affects taste discrimination. Imputed qualities may sometimes appear to be irrational, but they are of real importance. Mr. Pickard described statistical methods of market research which are relevant to ascertaining consumers' ideas of quality. The importance of directing research to the asking of the right questions was illustrated.

There was a short discussion at the end of each session and a general discussion on the last afternoon before Dr. A. J. Amos gave a final summing up.

It was evident that not all food technologists were expert in mathematics, and the suggestion naturally arose that opportunities should be provided for teaching them statistics. It was agreed that the various forms of quality control used should be explained to all production personnel. The colleges of food technology teach students these methods, but factory staff in general can best be reached by instruction given within their firms.

The advantages of early consultation with statisticians in the design of experiments was recognized. Co-operation between statisticians and food technologists might be necessary when using the less-simple techniques and both should know something of the others' subject. In some factories quality control has led to the elimination of excessive overweight once necessary to compensate for possible inaccuracies, and reduced costings have more than offset the cost of control.

Fatigue and bias among tasters were discussed. For some routine purposes fatigue did not reach critical importance, but where special discrimination was needed the number of samples compared should be small, possibly not more than two or three at a session.

In checking the composition of products such as jams or meat or fish pastes, analysts allow for some variation in the composition of raw materials. Manufacturers sometimes find that quite genuine raw materials occasionally fall short of the usual lower limits for some characteristic, and they suggest that analysts should therefore take wider limits as a basis for their calculations. Public analysts, on the contrary, suggest that raw material should not be used if it is of abnormally poor quality, however genuine. A fear was expressed that the setting of minimum standards may cause a decline of average quality towards that minimum. Although it was suggested that the need for standards was sometimes over-emphasized, the general view seemed to be that standards usefully show what the most indiscriminating customer has a right to expect, but do not necessarily represent what the discriminating customer wants. The manufacturer may be tempted by the complaisant consumer into a debasement of quality, and the analyst must strengthen the resolution not to succumb. Some quality-conscious people may be difficult to satisfy because their tastes are not sufficiently widely shared. It would be regrettable if standardization, in protecting the heedless, reduces the competition between manufacturers, thus depriving the good housewife of the pleasure of exercising individual skilful selection.

This symposium undoubtedly helped participants to realize that both public analysts and food manufacturers are interested in their own ways in service to the public. Co-existence may be the happier as a result of better appreciation of the reasons underlying each other's actions.

BIOCLIMATOLOGY AND BIOMETEOROLOGY

THE International Society for Bioclimatology and Biometeorology, which was founded in 1956 for the purpose of bringing together all kinds of people interested in the effects of climate on life, held its first congress in Vienna during September 23–27. The congress was attended by about one hundred scientists from most parts of the world, and it provided an opportunity for set talks on selected topics, short communications and lively discussions.

One of the aspects of climate which has been so far little-understood is ionization of the atmosphere. The term itself is vague, and it was obvious that ionization could mean cosmic rays, or normal components of the air electrically charged, or small suspended particles of the order of 0·1μ in diameter which can be detected by their electrical charges, or even ordinary dust. Experiments to study how specific sensations are related to ionization are difficult to control, but some work in the United States has suggested that sensations of 'stuffiness' in rooms are connected with ionization of the air, and good evidence was presented that attacks of bronchial asthma are related not so much to the presence of allergens in the air as to the simultaneous presence of allergens and certain conditions of ionization. Contributions on this subject by Dr. J. C. Beckett, of San Francisco, Dr. I. H. Kornblueh, of the University of Pennsylvania, and Dr. S. W. Tromp, of Leyden, made it seem probable that this may develop into an exciting field of investigation, not into an outlet for cranks smelling electricity.

Zoologists and botanists are becoming increasingly concerned with microclimate and its effects on life. Thus the temperature, humidity, air movement and heat radiation near the ground can be so widely different from conditions prevailing near the tree-tops in a forest that it is useless to consider only the climate of a forest as a whole, and microclimate must be studied in detail. Dr. R. B. Platt, of Emory University, Georgia, provided data about gradients of temperature and humidity in woods and in open fields, and Dr. V. Pasak, from Czechoslovakia, presented evidence that weeds growing in neglected woodlands interfere with the growth of new trees by their unfavourable effects on the microclimate near the soil. Outstanding among the zoologists' contributions was a well-illustrated account by Dr. R. C. Rainey, of London, of locust migration in Africa, which showed that the only relevant factor in directing locusts towards one area or another is the wind, while the insects in the swarm fly about apparently aimlessly and in circles. Another valuable contribution originating in Africa was that of Dr. Cloudsley-Thompson, of the Department of Zoology, King's College, London, who has studied the behaviour of some terrestrial arthropods which, like woodlice, lose water easily, and who produced evidence that the habits and habitats of such arthropods are related to their needs for preserving body water.

The tremendous possibilities for bioclimatological studies in tropical veterinary medicine were skilfully reviewed by Dr. J. D. Findlay, of Ayr, Scotland, who showed how milk yields could suffer at high temperatures and described some of the physiological work carried out at the Hannah Dairy Research Institute in Ayr, while another stimulating talk by Dr. R. Koller, from Austria, reviewed the problem in relation to animal husbandry in a temperate country with a cold winter and concluded that cattle did better, on the whole, in stables than out of doors when the weather was cool.

A particularly valuable aspect of such a conference is the possibility of discussing intricate problems which have a bearing on several fields of research. Town planning in relation to climate is such a problem, and outstanding contributions about this came from Dr. Vigan, of France, who discussed plans for workers' cities being built in the Sahara, and from Mr. Page, of the University of Liverpool, who surveyed problems of environmental comfort in houses not only from the engineering, physiological and æsthetic aspects, but also in relation to what is considered comfortable by different people. An interesting point made by Dr. Vigan, in reply to a question, was that trapical neuroses are infrequent among workers in the Sahara; this he attributed to the fact that the workers were there to do a useful job (though this could be connected with the fact that the weather in the Sahara is less uniformly warm than in equatorial regions, where neuroses are common).

The problem of adaptation to environment was approached in several ways. Prof. Pichotka, of Germany, showed not only that slices of potato metabolized at a lower rate in a cool medium than in a warm one, but also that they continued at a lower metabolic rate after leaving the cool medium, or at a higher rate after leaving the warm medium. This was particularly interesting, because these findings, obtained in cross-over experiments, resembled similarly crossed-over data obtained in mice and men and presented by Dr. J. S. Weiner, of the Medical Research Council Climate and Working Efficiency Laboratories, Oxford, who showed, among other things, that mice reared in a hot environment survive heat stress better than those reared in a temperate one. Though some adaptations, especially those in potato slices, must be brought about by changes in enzyme systems, the central nervous system appears to play a fundamental part in adaptation to climate in man, and evidence about this was presented by Dr. E. M. Glaser, of the London Hospital Medical College. Other evidence which implied the existence of central nervous adaptation came from Dr. H. Jungmann, of Germany, and Dr. M. Halhuber, of Austria, who had jointly studied acclimatization in the Alps at moderately high altitudes.

When considering the general effects of weather on health and sensations, speakers were perhaps on slightly more shaky ground, and this was forcibly pointed out by several speakers, including Prof. H. Berg, of Germany, one of the vice-presidents of the Society. Statistical evidence was produced, for example, that certain conditions, such as emboli of the heart, are more frequent in some than in other kinds of weather, but both the material and its statistical treatment were inconsistent, and the very definitions of the weather with which the clinical findings have been correlated were unsatisfactory. This branch of bioclimatology suffers, more than any other, from obscure terminology and meaningless notions such as 'sensitivity to weather' (*Wetterfühligkeit*), 'vagotonia' or 'meteorological fronts'. But the congress did some good in discouraging notions or lines of research which are unintelligible

without an excess of imagination. One of the most valuable aspects of the congress was that it provided an opportunity of revising fundamental notions borrowed from other branches of science which have been modified or invalidated by recent work.

The chairman of the congress was Dr. Fred Sargent, professor of physiology in the University of Illinois (who is now spending one year at the Medical Research Council Climate and Working Efficiency Research Unit in Oxford). Dr. J. L. Cloudsley-Thompson, of the Department of Zoology, King's College, London, was elected to the Council of the Society. The Society has begun publishing the *International Journal of Bioclimatology and Biometeorology*, and the proceedings of its first congress will appear in that journal. The second international congress of bioclimatology will be held in 1960, and England and Scotland have been mentioned as possible places for it. Information about the Society can be obtained from its secretary, Dr. S. W. Tromp, Hofbrouckerlaan 54, Oegstgeest, Leyden, Holland, or from its representative in Great Britain, Dr. E. M. Glaser, Department of Physiology, London Hospital Medical College, Turner Street, E.1. Candidates for election must be actively engaged in some field of bioclimatology or biometeorology, they must be proposed by two members, and they must be approved by the Council. The business of the Society is transacted mostly in English.

E. M. GLASER

TRANSISTOR TECHNOLOGY

A CONFERENCE on transistors, organized by the Electronics Group of the Institute of Physics, was held at the Brunel College of Technology, Acton, during September 27–28.

In almost every field of endeavour, the rate of progress largely depends on the facilities that exist for discussion and for exchanging information. This is particularly true when the available resources are scattered over a large number of industries, government and educational organizations, as is the case with the work on transistors. In the United States, professional societies and educational establishments seem to delight in organizing symposia and conferences, whereas in Britain there appears to be less inclination for activities of this kind; one hopes, therefore, that the success of this conference will provide a suitable stimulus to others.

Dr. M. E. Haine, chairman of the Electronics Group, explained that the topics had been chosen in such a way as to provide a broad picture of the wide range of activities that are embraced by transistor technology. Thus, the conference was less concerned with thrashing out points of detail than with providing an opportunity for those who are concerned with the details themselves to see a general picture.

The first paper, on "The Effect of Physical Properties of a Semiconductor on Device Characteristics", was given by Mr. D. D. Jones (General Electric Co.). In discussing the high-frequency performance of alloy transistors, he showed that the mobilities of both the majority and the minority carriers must be taken into account; the relative merits of *n-p-n* and *p-n-p* structures largely depend on the degree of avalanche multiplication that is characteristic of the carrier-depletion regions of thin collector junctions. Mr. Jones indicated which physical properties are important in the design of high-speed switching transistors and of power transistors. He also discussed the relative merits of germanium and silicon as transistor materials.

In the next paper, Dr. W. Bardsley (Royal Radar Establishment) discussed "Defects in Transistor Materials", and, in particular, mentioned the effects of chemical impurities, particle bombardment, and dislocations in the crystal structure. A typical chemical defect, that can have a marked effect on the electrical performance of the semiconductor, is the presence of oxygen in silicon. Defects created by particle bombardment, for example, by means of neutrons, can often be removed by annealing. Dr. Bardsley described various techniques, such as etching and the use of X-rays, for revealing the presence of dislocations in crystals. Finally, he spoke of interactions between defects; thus interactions between dislocations and oxygen content can affect the heat treatment properties of silicon.

Mr. J. G. Cressell (Marconi) opened his paper on "Power Transistors" by recounting the main steps by which progress has been made in this field. First, there was Webster's analysis of the variation of current gain with emitter current, which showed how emitter efficiency, bulk recombination and surface recombination play their part. The development of new alloys to give high emitter efficiency and of techniques to produce thin base regions were two practical steps of major importance. Fletcher's study of the transverse field in the base region led to a reconsideration of the optimum geometrical arrangement. Mr. Cressell then described how both carrier life-time and surface recombination velocity can show substantial variations with emitter current, and how these effects become important in high-power transistors.

The design of high-frequency transistors presents a considerable challenge. In describing "A New High-frequency Germanium Transistor", Mr. J. S. Lamming (General Electric Co.) first discussed the principle of Kroemer's drift transistor; in this a gradation in the conductivity of the base region creates a drift field which reduces the transit-time for minority carriers. One of the most attractive ways of producing a graded base region is to diffuse the impurity atoms into the region. In Mr. Lamming's technique of 'post-alloy diffusion' the emitter is alloyed on to a base region of uniform conductivity. The emitter alloy is made to contain known quantities of *p* and *n* impurities, the segregation and diffusion coefficients of which are carefully chosen. After alloying, the emitter is *p*-type. The structure is then heated to such a temperature that diffusion takes place, the coefficients being such that the diffusion is predominantly that of the *n* impurities. This technique enables very narrow base regions, with the desired gradation of conductivity, to be achieved.

Dr. J. T. Kendall (Texas Instruments) reviewed the situation of "Silicon Transistors". He mentioned how the difficulty in producing silicon of adequate purity and of keeping it pure during subsequent processing had delayed the development of these devices. The alloy process, so successful with germanium, had proved difficult with silicon and, as a result, most of the progress has been achieved with other processes, such as double-doping during crystal

growing, grown-diffusion, melt-back diffusion, and double-diffusion. Dr. Kendall also made an objective comparison of silicon and germanium transistors, stressing the advantages of the former in high-temperature applications.

In a conference where one often heard of the need for semiconductor materials of high quality, it was interesting to hear of some of the chemist's difficulties in Mr. J. M. Wilson's (Standard Telephone Laboratories) paper on "The Preparation of Very High Purity Silicon". The high segregation coefficient of boron makes it very difficult to purify by means of the zone-refining technique, which has been used so successfully with germanium. After reviewing a number of methods, Mr. Wilson described his work on a process which starts with the thermal decomposition of silane (SiH_4). The silicon can be produced in a crystalline form without having to use crucibles; this feature is attractive in view of the high reactivity of silicon with the crucible materials.

Dr. A. F. Gibson (Royal Radar Establishment) dealt with "Avalanche Injection" and the possibility of utilizing it in certain devices. When the field across a filament of n-type germanium exceeds a critical value, avalanche multiplication gives rise to a rapid increase in conductivity; as a result, the voltage–current characteristic exhibits a negative resistance region, similar to that obtained with a gas discharge tube. In order to limit the current, and hence the dissipation, in the high-current condition, the area of one of the contacts to the germanium is made small. Dr. Gibson then discussed a device, having two $n+$ contacts and one $p+$ contact to the germanium, which is analogous to the thyratron, and in which the current flowing into the $p+$ contact controls the voltage-current characteristic at the other two.

Dr. D. F. Taylor (Ferranti), in a paper on "Improved Junction Fabrication", dealt mainly with the problems of making alloyed junctions in silicon. He considered the conditions that are necessary for regrowth to take place. He showed that, when alloying an aluminium wire to a silicon wafer, if, during the cooling cycle, the wire is maintained at a higher temperature than the molten region no regrowth takes place; Dr. Taylor suggested that the reason why good diode characteristics are obtained under these conditions is that diffusion takes place at the alloy/silicon interface during the alloying. Finally, he considered some aspects of the 'limited' type of alloy process, such as takes place when a small 'dot' is alloyed to a silicon wafer.

The last paper in the conference was given by Dr. M. Smollett (Mullard), whose subject was "Germanium Photo-transistors". After considering the creation of hole–electron pairs in germanium when light shines on it, he described the photo-electric properties, including the spectral response, of a p–n junction diode in which the p-region is made very thin. He then analysed the operation of the photo-transistor, which differs from the diode in that it can produce substantial multiplication of the current that is produced by the hole–electron pairs that are generated by the incident light. Possibly their main disadvantage is the fact that hole–electron pairs produced by thermal agitation also contribute to the output current; Dr. Smollett indicated ways of minimizing this.

Each paper was followed by a discussion, during which many useful and stimulating comments were made.

HERRING IN THE NORTH SEA

IN 1955 the East Anglian herring fishery failed. This is a drift-net fishery which exploits different populations during October and November, and its success is to a large extent dependent on the dates of the full moons which, though not propitious for the 1955 season, could not possibly provide the complete reason for the failure. However, several changes had taken place since the Second World War. In 1948 the Danes started trawling for young immature herring and they were followed by the Germans, Dutch and French. These 'industrial' herrings were used for processing into fish meal. While the catches were at first insignificant they increased enormously during the following seven years until the number of herrings trawled far outnumbered those caught during the East Anglian fishery. Another rapid development since 1951 was the trawl fishery for adult herring in the Channel and North Sea Southern Bight by German, French, Dutch, Belgian, Polish and Icelandic fishermen. The landings from this new fishery have led to what might appear to be a shift from the fish being landed by drifters to being landed by trawlers. Coincident with these changes in the fisheries there have been changes in the environment (for example, the amount of food (*Calanus*) available) and in the biological characters of the herrings (as, for example, the mean length at various ages and, apparently, age at first maturity).

In a recent fishery investigation, published under the title "On the Herring of the Southern North Sea"*, Dr. D. H. Cushing and Mr. A. C. Burd have attempted to sort out these complexities, about which fishery biologists and fishermen have strong and divided views.

Their paper consists of four parts, the first of which, by Dr. Cushing, is concerned with the homogeneity and character of the Southern Bight stocks. In the second part he considers the natural changes that have occurred in the populations, changes among others, in age distribution, length, nature of recruitment, in the environment and in the fishery. Part 3, by Mr. Burd, discusses the changes that can be ascribed to fishing, while in the last section Dr. Cushing considers the effect of fishing on the stock. It is impossible in a review of this length to discuss their evidence in detail, but it leads them to believe that, through the advance in maturity, the fish are caught sooner in their life and this reduces the older age-groups which, together with the southern North Sea and Channel trawl fishery, reduces the November East Anglian catches of older fish. The danger caused by 'industrial' fishing of immature herrings receives a verdict of 'not-proven'. These conclusions should be put in perspective by pointing out that Dr. W. C. Hodgson, and many of the fishermen themselves, believe that this 'industrial' fishing to the north provides at least part of the explanation of the failure, and probably a large part.

Perhaps the wisest words in this paper are in Mr. Michael Graham's preface: "Dogmatism is out of place in this subject, . . . and in addition, data on highly migratory fisheries are always difficult to interpret".

T. B. Bagenal

* Ministry of Agriculture, Fisheries and Food. Fishery Investigations. Series 2, Vol. 20, No. 11: On the Herring of the Southern North Sea. By D. H. Cushing and A. C. Burd. Pp. iv+31. (London: H.M. Stationery Office, 1957.) 8s. 6d. net.

VIGILANCE AND THE INSPECTION PROBLEM

A STUDY of continued alertness and its implications for examining work in industry has been made by W. P. Colquhoun, of the Applied Psychology Research Unit, Medical Research Council (*Personnel Management*, **39**, No. 341; September 1957).

Laboratory studies of vigilance tasks have demonstrated conclusively that the ability to detect small changes in a display declines considerably within thirty minutes of beginning a watch. Circumstances which have been shown to enhance the effect are the presence of ambient noise, high environmental temperature, and loss of sleep beforehand. Alterations in illumination of visual tasks do not prevent deterioration with time, but produce differences in the over-all level of efficiency. Differences in over-all efficiency have also been found to exist between individuals, and have not, so far, been accounted for. Individuals also vary in the extent of the time decrement they show, but this appears to be unrelated to initial ability. The effects of isolation of the observer have been shown to be deleterious; but, on the other hand, the presence of too many other people tends to distract the worker from his task.

Earlier researches investigated the effects of changes in the externally imposed conditions under which the task was performed; the importance of both environmental and motivational factors were discovered. More recently, interest has centred on the determinants of efficiency that are inherent in the work-situation. It has been shown that uneven spacing of the signals along the time-scale is one of the most important factors likely to cause loss of alertness during prolonged work.

Understanding of the causes of the decline in efficiency of signal detection with time is by no means complete. It is well known that 'mental' fatigue, a state that arises with continued performance of the same task, is characterized by a fall in work output, a widening of subjective tolerance and an increased variability in both accuracy and in the timing of responses. In the vigilance situation, responses are usually of the all-or-none variety, and work-output a difficult concept to apply; but a widening of subjective tolerances might result in an increased effective threshold to display changes, so that differences must be larger before they are detected.

Colquhoun reviews the extent to which these experimental findings are relevant to the practical problems of examination and checking in the factory itself.

The response required of the examiner is rather more elaborate than it is in the laboratory; thus he must either pick up the defective article and place it aside, sort the objects in some way, or mark the defective part of a large article with chalk or similar material. He may also be required to enter his observations on a work sheet. If the object is of any size or complexity he may have to manipulate it so that all parts of it are examined.

Noise, atmospheric conditions and lighting may be expected to vary widely between workplaces, as do the actual layouts of particular jobs. Though there are cases where the inspection is completely machine paced, more often the examiner has a degree of control over his speed of work which allows him to take rests in addition to those officially sanctioned. If a quality bonus system is in operation it becomes important not only to detect faults, but also to avoid rejecting good items.

Information about the efficiency of his work only reaches the examiner after a considerable time delay, either from subsequent check inspection, the occurrence of later processing faults or from customers' complaints.

The main difference in the internal structure of the tasks lies in the greatly increased number of signals, mainly 'unwanted' ones, that arrive in a given time.

It is quite common for one examiner to check thousands of items in a day's work, in which the number of rejects may vary from one to hundreds. Although the temporal occurrence of faults is unpredictable, the mean interval between them may sometimes be only of the order of seconds, as compared with the minutes usual in laboratory and military tasks. The accuracy of the discriminations required, on the other hand, may be extremely fine, but these fine discriminations may only be necessary at relatively infrequent intervals, particularly if the defect being sought varies in magnitude over a wide range. These latter factors in turn affect the nature of the response. It may not be sufficient for the examiner to divide the items into 'passes' and 'rejects'; he may be required to grade them into several categories, both of 'good' and 'bad', and also to sort them into kinds of defect. This kind of activity requires decision-taking and the exercise of judgment.

In inspection work only signals which fall outside given tolerance limits are responded to. Tolerance limits are normally laid down in the specification of the particular article being examined, but in many cases they can be varied from time to time to match fluctuations in general trade, or to suit the requirements of a particular customer. Here there is clearly room for a considerable degree of subjective estimation. It appears that the examiner's work is considerably more complex than is the subject's in the sort of task that has usually been set in experimental studies of vigilance. Relatively little study has in the past been devoted to the inspection problem from this point of view.

More information is needed on the effects of various conditions on inspection efficiency. To this end a device has been constructed at the Applied Psychology Research Unit of the Medical Research Council which presents a simulated visual examination task to the subject. The flexibility and comparative simplicity of the apparatus make it suitable for the study of a wide range of inspection problems which include:

(1) *Inherent task-conditions.* Under this heading it will be possible to investigate the effects on efficiency of varying: (*a*) the frequency of faults; (*b*) the type of fault; (*c*) the difficulty of the discrimination required; (*d*) the number of objects displayed simultaneously; (*e*) the number of dimensions on which the objects vary; (*f*) the temporal structure of the sequence of faults; (*g*) the distribution of faults of different kinds and degrees; (*h*) the 'meaningfulness' of the task, that is, the nature of the objects to be examined; (*i*) the number of classes into which the objects must be sorted; (*j*) the number and nature

of 'additional' operations required (for example, 'booking').

(2) *External conditions.* These include variables like: (*a*) the speed at which the task must be performed; (*b*) the total length of the task; (*c*) the frequency of the rest-pauses; (*d*) the effects of various kinds of interpolated activity during breaks on subsequent performance; (*e*) the degree of isolation of the subject; (*f*) illumination, contrast, noise and atmospheric conditions; (*g*) time of day or night, lack of sleep; (*h*) knowledge of results, that is, awareness of performance efficiency; (*i*) amount and nature of reward, that is, incentive systems; (*j*) presence or absence of objective reference standards, and their intermittent variation.

(3) *Individual variability.* It is predicted that subjects will vary widely in their performances. It is hoped to relate these differences to measures of intelligence and personality, and to the extent of previous experience at similar tasks.

It is hoped that initial experiments will disclose the more important conditions which can then be studied in more detail. The laboratory studies will be followed up, where possible, by actual observations 'on the job'. Any information on the efficiency of inspection would have a value for industry where inspection processes will rise as production becomes more automatic.

In order to ensure that people work at their maximum efficiency it is essential to understand both the nature of the inspection process and the optimum conditions under which it should be carried out.

DOSE-RATE EFFECTS IN RADIATION-INDUCED CHEMICAL REACTIONS

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THE initial stages of chemical reactions induced by ionizing radiations are usually assumed to be independent of the dose-rate. Thus, in the case of a simple reaction in aqueous solution, such as the oxidation of ferrous sulphate induced by high-energy radiations, the yield remains constant at the highest dose-rate hitherto studied[1], namely, 10^6 rads/sec. If, however, the radiation intensity is increased to such a degree that the reaction zones of clusters of radicals formed by neighbouring ionizing particles overlap, then the yield of the reaction should show a dose-rate dependence due to the increase of concentration of radicals. Dose-rates much higher than the above value can be produced in the travelling wave linear accelerator, in which the acceleration of electrons takes place in pulses of short duration.

The 15 MeV. linear accelerator at St. Bartholomew's Hospital[2] is capable of producing beams of electrons in pulses 1·3 μsec. wide, and at dose-rates up to 20,000 rads per pulse. A continuous variation of the dose-rate by a factor of 10^4 can be achieved by decreasing the current through the gun filament. Another facility provided in this machine is a variable repetition-rate of the pulses.

This accelerator was employed in an experiment to study the variation of yields of chemical reactions with dose-rate. Two reactions were studied: the reduction of aerated solutions of ceric ammonium sulphate in 0·8 *N* sulphuric acid, and the oxidation of ferrous ammonium sulphate in an identical solvent. Possible errors in dosimetry were avoided by passing the electron beam through a system of two cylindrical 'Pyrex' vessels, joined by a common wall. The rear vessel, which was always filled with ferrous sulphate, was employed as a chemical monitor, while the near vessel was alternatively filled with ceric and ferrous sulphate. In order to avoid errors associated with intensity variations across the beam, the diameter of the vessels was made considerably larger than the beam width. In consequence, the solutions were exposed to a range of dose-rates distributed in the same manner in each experiment. The dose-rate given in Fig. 1 is the energy-averaged value in the near vessel, during each pulse. The dose-rate at any point did not exceed twice this value, and more than 85 per cent of the total energy was delivered at dose-rates greater than 40 per cent of the average value. A dose of not more than 30,000 rads over the irradiated volume was delivered at a time. The number of pulses needed to give this dose varied from 1 to 10^4 depending on the dose-rate. When larger total doses were required the solutions were stirred between exposures. At each dose-rate the ratio of the yields of the iron and cerium reactions, G^{Fe}/G^{Ce}, was determined. The results are shown in Fig. 1, from which it is seen that this ratio decreases steadily, starting from a dose-rate of about 10^7 rads/sec.

We attribute this effect to an increase in radical concentration with increasing dose-rate resulting from the overlapping of the reaction zones of radical clusters. The following evidence supports this interpretation.

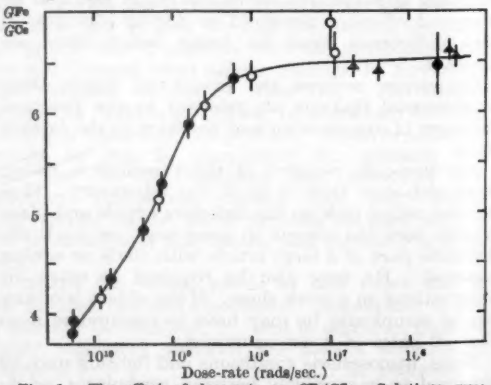

Fig. 1. The effect of dose-rate on G^{Fe}/G^{Ce}. Solutions were irradiated in vessels: 2 cm. diameter, ●; 5 cm. diameter, ○; and 1 cm. width in a uniform radiation field, ▲

(1) If such overlap occurs, then the yield of inter-radical reactions to form the molecular products hydrogen and hydrogen peroxide should increase with dose-rate, at the expense of radical–solute reactions. This would cause the ratio G^{Fe}/G^{Ce} to decrease with increasing dose-rate, as observed.

(2) The yield obtained with radiation of low ion density but high dose-rate should simulate that produced by radiation at a low dose-rate but high ion density. For X-rays producing secondary electrons of average energy of about 20 keV. a value of 4·9 for the ratio G^{Fe}/G^{Ce} has been observed[3]. At this low energy the ion density is approximately 16 ion clusters per micron of electron path, giving an initial mean distance between the centres of adjacent radical clusters in the same electron track of about 625 A. In our experiment this value of the ratio of G^{Fe}/G^{Ce} was observed at a dose-rate of 2,800 rads per pulse. Assuming a mean energy expenditure[4] per cluster of 110 eV., and that the mean life-time of the clusters is long compared with the pulse duration, we obtain a mean distance between cluster centres at the end of each pulse of 860 A., in good agreement with the above value.

(3) The assumed competition between radical–radical and radical–solute reactions in overlapping zones should be influenced by variations not only of dose-rates but also of solute concentrations. In confirmation of this we have observed (*a*) that the addition of 5×10^{-3} *M* cerous sulphate to a ceric sulphate solution before irradiation lowers G^{Ce} to 66 per cent of its normal value at 10^{10} rads/sec.; at dose-rates lower than 10^{7} rads/sec. the corresponding decrease was only to 93 per cent, and (*b*) if a ferrous sulphate solution is equilibrated with oxygen instead of air before irradiation, then G^{Fe} is raised by 13 per cent at $1{\cdot}3 \times 10^{10}$ rads/sec. as compared with 2·5 per cent at low dose-rates. Variations of the ceric ion and ferrous ion concentration have little effect. We conclude that the solute competing for hydroxyl radicals in the cerium system is cerous sulphate, at least when present in excess; and that the solute competing for hydrogen atoms is dissolved oxygen.

(4) It might be argued that accumulation of hydrogen peroxide at high dose-rates may be responsible for the variation of G^{Fe}/G^{Ce}. This is easily refuted by consideration of the life-time of hydrogen peroxide in the irradiated solution in relation to the total treatment time, and by the further observation (see below) that G^{Fe}/G^{Ce} is not influenced by variations of the interval between pulses.

In the experiment described, only the yield ratios of the two reactions could be determined. A method has since been developed, using a different type of irradiation vessel, to determine the variation of the two reactions separately. Preliminary results show that most of the observed variation with dose-rate is due to the cerium system. This is as to be expected, since a small fractional increase in the yields of the molecular products hydrogen and hydrogen peroxide would influence G^{Ce} more than G^{Fe}. This is also in accord with the observations mentioned under (3) above. A detailed study of the two systems is in progress.

Apart from establishing the dose-rate effect, these experiments enable us also to make some guesses about the life-times of the radicals. From considerations of the time required for radicals to diffuse the distance between clusters, we can obtain a minimum value for their life-time on the assumption that a reaction occurs at every collision of two radicals from neighbouring clusters. From the shape of the curve in Fig. 1, together with an assumed value for the diffusion coefficient of the radicals (2×10^{-5} cm.^{2} sec.$^{-1}$), we deduce that this minimum value is 0·5 μsec.; the actual value is probably much greater than this. On the other hand, from the observed fact that a variation of the pulse repetition-frequency from 400 per sec. to 1 per 20 sec. did not affect the value of the ratio G^{Fe}/G^{Ce}, we conclude that the radicals formed in one pulse must be destroyed in less than 1/400 sec.; this gives an upper limit for the life-time of 2·5 msec. Experiments are now in preparation to narrow down these limits.

These investigations form part of a programme of research carried out with the aid of grants provided by the Treasurer and the Board of Governors from the Discretionary Fund of St. Bartholomew's Hospital, to whom we wish to express our gratitude.

[1] Schuler, R. H., and Allen, A. O., *J. Chem. Phys.*, **24**, 56 (1956).
[2] Rotblat, J., *Nature*, **175**, 745 (1955).
[3] Hardwick, T. J., *Disc. Farad. Soc.*, **12**, 203 (1952).
[4] Pollard, E., "Advances in Biol. Med. Phys.", **3**, 153 (1953).

INSECTICIDE RESISTANCE IN *ANOPHELES SUNDAICUS*

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RESISTANCE to DDT in *Anopheles sundaicus* in Java was first reported by Crandell[1] in 1954 in an area where house-spraying with this insecticide had been carried out for the previous three years. Chow[2] later confirmed such resistance in another area, and I was privileged to visit the island in 1955 and report on the situation for the World Health Organization.

In July 1956, Prof. C. Y. Chow, World Health Organization entomologist, was kind enough to send to the Ross Institute in London eggs of DDT-resistant *A. sundaicus* from yet another area of Java where resistant mosquitoes had recently appeared. A thriving colony of this strain was soon established in London. Repeated attempts by Mr. S. Sundararaman, World Health Organization entomologist, to dispatch eggs of susceptible mosquitoes of the same species from Java to London met with no success, however. A susceptible strain of *A. sundaicus* was eventually obtained from Malaya, through the courtesy and repeated efforts of Mr. J. A. Reid of the Institute for Medical Research. Great difficulty was experienced in colonizing this susceptible strain, and it is only in recent weeks that sufficient numbers of mosquitoes have been reared to enable a solution of the problem of resistance in this species to be achieved.

Table 1. Median Lethal Concentrations (percentages in Risella Oil) of various Insecticides when Susceptible and Resistant Strains of *Anopheles sundaicus* are exposed for One Hour

Numbers of mosquitoes tested at concentrations giving more than 0 and less than 100 per cent mortalities are given in brackets

Insecticide	Susceptible		Resistant	
	Java strain (in Java)	Malaya strain (London colony)	Java strain (in Java)	Java strain (London colony)
DDT	0·5 (159)	0·3 (278)	9·0 (165)*	> 4·0 (565)
Dieldrin	0·065 (206)	0·032 (321)	0·08 (527)	0·038 (420)
Gamma-BHC	0·008 (86)	0·003 (290)	0·0085 (151)	0·006 (192)
Aldrin	0·37 (101)		0·4 (171)	

* Interpolated from logarithmic-probability graph from only two mortalities.

The two strains of the same species have now been compared for their susceptibilities to a range of insecticides using the technique described by Busvine in an annex to the Fifth Report of the World Health Organization Expert Committee on Malaria[2]. This technique involves the exposure of mosquitoes to filter paper impregnated with various concentrations of insecticides in Risella oil for 1 hr. and recording mortalities 24 hr. later. Table 1 records the median lethal concentrations of four insecticides after this 1-hr. exposure, both in the laboratory colonies and in the field.

The resistant strain is seen to be resistant to DDT but not to the other three insecticides. The differences between the field and laboratory results can be accounted for by the fact that, in the field, wild-caught, blood-fed, semi-gravid and gravid females were used for the tests, while in the laboratory the more susceptible unfed females and males were used.

In addition to these insecticides, laboratory-reared mosquitoes of the two strains were exposed to three DDT-analogues with the following percentage mortalities (numbers of mosquitoes exposed are given in brackets):

Table 2

Insecticides	Susceptible	Resistant
1 per cent methoxychlor	89 (36)	24 (39)
2 per cent dichloro-diphenyl-dichloroethane ('Rhothane')	100 (27)	3 (37)
4 per cent diethyl-diphenyl-dichloroethane ('Perthane')	100 (18)	16 (25)

Like the DDT-resistant strains of other insect species, then, cross-resistance extends to closely related compounds but not to the cyclodiene compounds, dieldrin, aldrin, etc., or to BHC.

The degree of resistance to DDT in *A. sundaicus* is considerably less than that of *A. gambiae* to dieldrin[4]. According to Crandell[1], it is of the order of twenty-five times. From my estimations in Java it was of the order of eighteen times. A comparison of the Malayan and Javanese laboratory colonies in London indicates a resistance of some forty times. 103 mosquitoes of the Malayan strain showed a 50 per cent mortality after exposure to 0·1 per cent DDT for 2 hr., and 255 mosquitoes of the Javanese resistant strain showed a 58 per cent mortality after an exposure of 2 hr. to 4 per cent DDT.

Reciprocal crosses between the laboratory-susceptible and resistant strains produce hybrids only slightly more resistant than the susceptible strain (see Table 3). It was not possible, therefore, to choose a discriminating dosage of the insecticide which would kill susceptibles and not hybrids, as it was with dieldrin-resistant *A. gambiae*[5]. What was possible, however, was to choose one discriminating dosage, 2·5 per cent DDT, which would kill almost all susceptibles and hybrids but very few of the resistant strain (see Table 3).

Unlike most of the *A. gambiae* hybrids[5], *A. sundaicus* hybrids readily interbreed. The F_2 generations exposed to the discriminating dosage show an approximate 75 per cent kill (Table 3), indicating simple Mendelian inheritance. This has been confirmed by back-crossing the hybrids with the susceptible and resistant parent strains. The offspring of the back-crosses to the resistant parent showed approximately the expected 50 per cent kill after exposure to the discriminating dosage. The offspring of the back-crosses to the susceptible parent showed an almost complete kill (Table 3).

These findings indicate that this resistance is inherited by a simple monofactorial mechanism. One homozygote displays a marked resistance. The heterozygote resembles the susceptible homozygote, resistance being virtually recessive. Only two degrees of susceptibility or resistance can therefore be found, whereas in the dieldrin-BHC-resistant *A. gambiae* three phenotypes were found. It is almost certain that the heterozygote *A. sundaicus* would be killed by field dosages of the insecticide and this may explain why DDT-resistance in anophelines has always been much slower to appear in the field than was dieldrin-BHC-resistance in *A. gambiae*, where the hybrids, themselves being significantly resistant, almost certainly survive.

Resistance to DDT which has these characteristics would probably not be detectable when homozygote

Table 3. Mortalities at Varying Percentages of DDT in Risella Oil among Susceptible, Resistant, Hybrid, Interbred Hybrid and Backcross Offspring of *A. sundaicus*

Numbers of mosquitoes tested are given in brackets

Percentage DDT in Risella oil	Susceptible strain (*S*)	Resistant strain (*R*)	Hybrid I $R♂ \times S♀$	Hybrid II $S♂ \times R♀$	Offspring of Hybrid I	Offspring of Hybrid II	Backcross $R♂ \times$ Hybrid II♀	Backcross Hybrid II$♂ \times R♀$	Backcross $R♂ \times$ Hybrid I♀	Backcross $S♂ \times$ Hybrid II♀	Backcross Hybrid II$♂ \times S♀$
0·25					37 (359)						
0·5	73 (67)		31 (39)		56 (120)	16 (43)	6 (47)	18 (40)	3 (30)		
1·0	100 (47)	0 (63)		39 (70)	70 (67)	33 (45)	29 (24)				
1·5	100 (22)			76 (68)	70 (40)	58 (33)	31 (26)				
2·0	98 (56)	8 (84)	80 (54)	97 (123)	82 (70)	67 (45)	48 (23)				
2·5	93 (86)	3 (39)	98 (61)	99 (236)	82 (176)	74 (265)	53 (126)	56 (206)		95 (218)	94 (69)
3·0		10 (59)			87 (74)						
4·0		8 (383)			81 (107)	76 (51)	51 (41)	67 (33)	41 (27)		
Check	2 (62)	4 (267)	9 (35)	4 (48)	4 (113)	3 (32)	0 (29)	11 (28)	0 (16)	5 (22)	13 (16)

The dotted line indicates the discriminating dosage, 2·5 per cent DDT, which kills hybrids and susceptibles but not resistants

resistant members were few in number, because hybrids cannot in practice be identified. Moreover, a female, suspected to be homozygote resistant, but caught in Nature after fertilization by an unknown male, might produce apparently susceptible progeny. If the mother were resistant this progeny would correspond to one of the following groupings: 100 per cent resistant; 50 per cent resistant and 50 per cent hybrid; and 100 per cent hybrid; and the last of these, all succumbing to the discriminating dose, might give the impression that they were derived from two susceptible parents. An F_2 generation derived from them would include 25 per cent resistant, 50 per cent hybrid, and 25 per cent susceptible members. The resistant members would be detectable, and their ancestry could be traced from this generation. In field observations, therefore, the presence of many survivors of a discriminating dose would indicate resistance, and the presence of a few would give rise to a suspicion of it, to be followed by the rearing and testing of progeny from them, and if possible the rearing and resting of a second generation.

I gratefully acknowledge the assistance given me by Miss C. E. Jackson and the skill and untiring work of Miss W. J. Wall and the technicians of this Institute, whose efforts overcame the great difficulties in establishment of the colonies studied.

[1] Crandell, H. A., *Mosquito News*, **14**, 194 (1954).
[2] Chow, C. Y., and Soeparmo, H. T., *Bull. World Health Org.*, **15**, 785 (1956).
[3] World Health Organization Tech. Series Report No. 80 (1954).
[4] Davidson, G., *Nature*, **178**, 705 (1956).
[5] Davidson, G., *Nature*, **178**, 863 (1956).

FLUORESCENCE MICROSCOPY IN THE STUDY OF NUCLEIC ACIDS

Histochemical Observations on Cellular and Virus Nucleic Acids

RECENT inquiry into the histochemical significance of tissue fluorescence induced by acridine fluorochromes[1] led us to consider the possibilities of this aspect of fluorescence microscopy for studies on the intracellular phase of virus infection. If thin sections of Carnoy-fixed animal tissues are treated with a dilute and suitably buffered solution of acridine orange (or its 5-phenyl derivative, acridine orange *R*) it is possible with the fluorescence microscope to identify readily the distribution of nucleic acids within the tissue, and further, to distinguish between ribonucleic acid and deoxyribonucleic acid. Normal tissues prepared in this way acquire strong polychromatic fluorescent properties, best activated by irradiation with intense blue-violet light. With acridine orange in the *p*H range of 1·5–3·5, nuclear chromatin containing deoxyribonucleic acid emits strong greenish-yellow fluorescence, while a characteristic flame-red colour is seen in those parts of the cell cytoplasm and in the nucleolus which have an appreciable content of ribonucleic acid. With acridine orange *R*, corresponding results are obtained in the *p*H range of 3·5–5·0.

The connexion between the normal components of the host cell and infective virus material forms one of the central problems in virus research. It is now recognized that all viruses contain either deoxyribonucleic or ribonucleic acid as an essential constituent, and it therefore seemed possible that the acridine fluorescence technique could be utilized for revealing significant cytochemical changes during the phase of virus multiplication. Preliminary findings with some viruses of widely different character are reported here. Observations on two virus diseases of *Tipula paludosa* were possible through the kindness of Dr. Kenneth M. Smith, who provided us with some infected larvæ; the structure of both viruses has been studied recently by Dr. Smith and his collaborators with the electron microscope. *Tipula* iridescent virus[2] is a crystallizable agent containing deoxyribonucleic acid producing gross lesions of the larval fat body. With the acridine orange technique, the cytoplasm of cells in the affected region of the fat body was seen to be distended with granular material emitting strong greenish-yellow fluorescence of the deoxyribonucleic acid type. Traces of the same material occurred in the body cavity of the larva, and abundantly in the cytoplasm of most of the epidermal cells of the body wall. Since deoxyribonucleic acid is not a normal constituent of cell cytoplasm, it is reasonable to suspect that accumulations of virus material containing deoxyribonucleic acid may account for this remarkable appearance. There was no obvious primary change in the cell nuclei other than enlargement of the nucleolus, which fluoresced a brilliant red. In larvæ infected with *Tipula polyhedrosis*, on the other hand, profound changes do occur in the nuclei. The cells chiefly involved are the hæmocytes of the blood.

Electron microscopy[3] has shown that virus rods appear in the cell nucleus and later accumulate within oval masses adherent to the nuclear membrane which are eventually discharged from the cell in the form of crescentic polyhedra or 'crystals'. In blood smears and whole sections through an infected larva examined with the fluorescence technique, few normal hæmocytes were present and the blood contained a profusion of crescentic, refractile polyhedra. In the least-affected blood cells there was an unusually dense network of intra-nuclear material showing strong greenish-yellow fluorescence, together with one or more spherical and homogeneous bodies emitting similar fluorescence of the deoxyribonucleic acid type. In other cells, part of the fluorescing material had become segregated to form bright greenish-yellow masses, oval in outline and attached to the nuclear membrane. A later stage is represented by cells in which the structures containing deoxyribonucleic acid had come to lie within the red fluorescing cell cytoplasm, but their homogeneous character was now lost and intense yellowish fluorescence restricted to their inner border, that is, the surface last in contact with the nuclear membrane. Extracellular polyhedra were outlined prominently as blue dark-ground images, showing only weak yellowish fluorescence.

These observations with the fluorescence microscope appear to present visible evidence of the incorporation of nuclear deoxyribonucleic acid into a remarkable and complex pattern of virus formation and are broadly in accord with the evidence of electron microscopy. It was also noted, however, that only a part of the abnormal deoxyribonucleic acid seems to be utilized for the developing polyhedra; much of it remains in granular form within the nuclear membrane and is released into the blood on disintegration of the cell.

Two members of the pox group, vaccinia and mouse ectromelia, have also given interesting results with the acridine orange technique. As expected on account of their known content of deoxyribonucleic acid, the elementary bodies in purified vaccinia preparations, for which we are indebted to Dr. D. McClean, exhibited greenish-yellow fluorescence, the fluorescent material being concentrated in the centre of each virus particle. Similarly in the liver cells of mice infected with ectromelia greenish-yellow bodies, varying from about 0·25μ to 1·0μ in diameter, were demonstrable in the cytoplasm of cells, most of which showed no other abnormality and looked quite normal in routine histological preparations. A quite different appearance was found in the liver of mice infected with mouse hepatitis virus[4]; here the hepatic cells at an early stage of infection contained abnormal accumulations of material fluorescing intensely red (ribonucleic acid) in their cytoplasm. In this instance, there is at present no biochemical evidence concerning the type of nucleic acid in the virus and the identity of the material containing ribonucleic acid is an open question.

The interpretation of an altered pattern of fluorescence in cells following virus infection is a complex problem, since changes in the amount and distribution of the host cell's own nucleic acids will almost inevitably accompany or result from the intracellular multiplication of virus, and histochemical evidence must, where possible, be correlated with that obtained with the electron microscope and from biochemical studies. The feasibility of distinguishing histologically between virus and cellular nucleic acids is suggested by experiments on their susceptibility to digestion by the specific nucleases. It was noted that the abnormal material containing deoxyribonucleic acid in the fat body cells of larvæ infected with *Tipula* iridescent virus was resistant to direct digestion by crystalline deoxyribonuclease, although the normal nuclear deoxyribonucleic acid of all cells in the test specimen was completely removed with consequent loss of the specific greenish-yellow fluorescence. Similar resistance was shown by the deoxyribonucleic acid of vaccinia and by the hepatic inclusions in ectromelia. Pre-treatment of the sections with 0·02 per cent pepsin at *p*H 2·0 for 2 hr. at 37° C. (which did not itself inhibit the specific deoxyribonucleic acid fluorescence) rendered the deoxyribonucleic acid susceptible to subsequent digestion by the specific nuclease. These findings parallel observations with the electron microscope on influenza and other myxoviruses[5], which showed that nuclease treatment did not affect the electron density of the virus particles unless preceded by treatment with a proteolytic enzyme. In the case of *Tipula polyhedrosis*, however, pre-treatment with pepsin had no such unmasking effect on the deoxyribonucleic acid of the infected blood cells and its nuclease resistance remained unbroken. There is at present insufficient evidence to indicate that nuclease resistance is likely to be encountered in all viruses, or at what stage in the formation of virus such protection is afforded to its nucleic acid. It is interesting to speculate on the possibility that a high degree of nuclease resistance, surviving even treatment with pepsin as in the case of *Tipula polyhedrosis*, may be a feature of an intra-nuclear site of virus formation.

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[1] Armstrong, J. A., *Exp. Cell. Res.*, **11**, 640 (1956).
[2] Williams, R. C., and Smith, K. M., *Nature*, **174**, 562 (1954).
[3] Smith, K. M., *Parasitology*, **45**, 482 (1955).
[4] Dick, G. W. A., Niven, J. S. F., and Gledhill, A. W., *Brit. J. Exp. Path.*, **37**, 90 (1956).
[5] Valentine, R. C., and Isaacs, A., *J. Gen. Microbiol.*, **16**, 195 (1957); *ibid.*, **16**, 680 (1957).

Visual Observation of Deoxyribonucleic Acid Changes in Bacteria during Growth of Bacteriophage

Armstrong[1] demonstrated the specific fluorescences of ribonucleic acid and deoxyribonucleic acid when stained with acridine orange and, in collaboration with Niven[2], has now shown that such fluorescence can be used for following the development of virus nucleic acids in animal tissues. This prompted me to investigate the practicability of using the method to follow the development of deoxyribonucleic acid in bacteria during the growth of phage. A lysogenic culture of *S. typhi*, *Vi*-phage type *D6*, which carries type-determining phage d_6[3,4], was chosen as the test organism. The culture was exposed to ultra-violet radiation for 5 sec. in buffer solution at *p*H 7·0, 45 cm. from a 30 W. B.T.H. germicidal low-pressure mercury vapour lamp. This procedure has previously been shown to result in induction of more than 99 per cent of cells. An equal volume of double-strength nutrient broth was added to the irradiated cells and the resulting suspension was incubated at 37° C. The irradiated culture was also inoculated on to nutrient agar, which was incubated similarly. Sampling was carried out before and immediately after irradiation, and afterwards at 15, 30, 45, 60, 90, 120 and 180 min. Smears made on chemically cleaned slides were stained with Gurr's acridine orange at *p*H 5·0 and were examined by dark-ground fluorescence microscopy, the method being, with slight modifications, similar to that of Armstrong[1]. In our preparations the ribonucleic acid fluoresced red and the deoxyribonucleic acid yellow-green. The colour filters were adjusted so that a faint blue-green dark-ground image of the cell walls was visible. The nuclei were very distinct in uninduced (control) cells, and showed as bright subterminal yellow-green rods of morphology similar to that described by numerous workers (Fig. 1*A*). Most cells in the logarithmic phase of growth were binucleate, but organisms with four or more nuclei were common. When the nuclei were about to divide, the intensity of nuclear fluorescence increased and the rods became thicker and then separated into two, the separation often commencing at one nuclear pole, so that the familiar V formation was apparent.

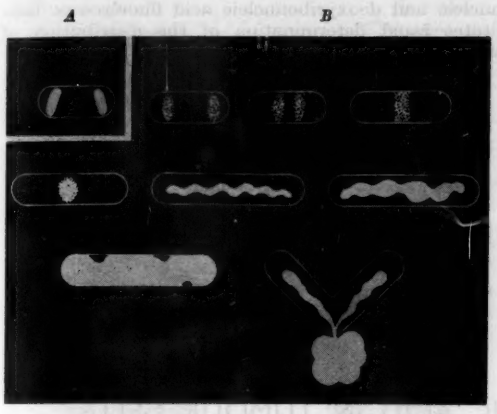

Fig. 1. *A*, normal cell of *Salmonella typhi*, type *D6*; *B*, changes observed in type *D6* after ultra-violet irradiation. Left to right: 5–15 min., 5–15 min., 15–30 min., 15–30 min., 30–45 min., 30–45 min., 45–60 min., 60 min. onwards

Fig. 1*B* is a diagrammatic representation of the sequence of events observed after irradiation. Within a few minutes the nuclear fluorescence was less intense and the nuclei became less compact, so that their long axes were no longer so clearly transverse. Where nuclei had recently divided but were still close to each other, their outlines soon fused with one another. Subterminal nuclei migrated to the centre of the cell, there to fuse into a single, rather dimly fluorescent mass of deoxyribonucleic acid. In longer cells which were quadrinucleate, that is, were probably in the process of dividing, the pairs of nuclei behaved as if they belonged to independent cells and fused into two masses, situated at the junctions of the thirds of the bacteria. The process of nuclear migration and fusion was well advanced within 15 min. of irradiation and was substantially complete after 30 min. Between 15 and 30 min. the central deoxyribonucleic acid mass became somewhat more compact and exhibited brighter fluorescence. At 30 min. many cells showed a fine axial filament of deoxyribonucleic acid, often wavy in outline, extending towards the bacterial poles on each side of the central mass. These filaments thickened and increased in brightness; 45 min. after induction, the great majority of bacteria showed such filaments, which had greatly increased in thickness and brilliance; their outline remained wavy or became heavily beaded. As the filaments thickened the central deoxyribonucleic acid mass disappeared. Although obvious division of the bacteria could rarely be found in the irradiated culture, increase in cell length took place, and by 45 min. after irradiation the mean cell length had almost doubled.

After 1 hr. most cells were virtually filled with deoxyribonucleic acid although the beading referred to above persisted. From this time onwards, cells in various stages of bursting were frequently seen. Although the actual rupture may have been due to the effect of making the smears on already fragile cells, it is nevertheless worth while recording its course. At first a localized bulge of the cell wall could be seen into which projected a small finger of deoxyribonucleic acid. The bulge increased in size until the wall ruptured and the deoxyribonucleic acid escaped; once this had occurred the brilliance of the deoxyribonucleic acid fluorescence increased considerably. In the early stages the extracellular deoxyribonucleic acid could clearly be seen to be attached to that still within the cell, and the latter diminished *pari passu* with the increase in amount of the former. Finally, all the deoxyribonucleic acid was extracellular and the empty cell was visible only as a faint dark-ground image.

Bursting cells were common from 1 hr. onwards after irradiation and their increase in number coincided with the rise in phage titre in liquid medium, the maximum of both being reached in about 1½–2 hr. after irradiation. At this time also, visible lysis occurred in the liquid medium, the resulting liquid exhibiting distinct birefringence, presumably due to the liberation of an excess of free deoxyribonucleic acid.

Two types of body made their appearance in smears prepared during and after the lysis period. The first showed as a pure dark-ground image, circular in outline, and about 0·2–0·3μ in diameter. The second fluoresced faintly as deoxyribonucleic acid and was circular or oval, with a long axis of about 0·5μ. The nature of these bodies, which became numerous when lysis was well advanced, is not yet known. When the primary (blue) filter was removed, so that the preparation could be examined by ordinary dark-field illumination, numerous small bodies, which showed only as dark-ground images, could be seen embedded in the deoxyribonucleic acid released from ruptured cells.

Three hours after irradiation, normal cells were reappearing and they afterwards increased in numbers to some extent, although the culture never reached an opacity of more than about one-quarter of that of the unirradiated controls.

Irradiation of a strain of *Vi*-phage type *A* of *S. typhi*, in which we have not so far been able to demonstrate lysogenicity, resulted in changes of a similar nature only up to the point of central migration and fusion of the nuclear deoxyribonucleic acid. The type *A* culture was lysogenized with phage d_6, the temperate determining phage carried by the type *D6* strain referred to earlier. This procedure converts type *A* into type $D6^{s,4}$. Control samples of the new lysogenic strain showed the same nuclear appearances as the parent type *A*. After ultra-violet induction the train of events was closely similar to that already described in irradiated type *D6*, and many bursting cells releasing brightly fluorescent deoxyribonucleic acid were found from 1 hr. onwards after irradiation. Thus, the differences in deoxyribonucleic acid production in the lysogenized irradiated, as compared with the unlysogenized irradiated, culture were evidently connected with the presence of prophage d_6 in the cells.

The progress of infection of bacteria with a virulent phage has also been followed by this method; the changes in deoxyribonucleic acid have similarities to those outlined for the induced lysogenic culture, but will not be given in detail here.

Smears of a purified pellet of *Vi*-phage II, suspended in a minimum of buffer, fluoresced yellow-green after staining with acridine orange. Preparations of normal bacteria, of induced lysogenic cells and of free phage, treated with deoxyribonuclease after fixation but before staining, did not show the yellow-green fluorescence characteristic of deoxyribonucleic acid. This is in contrast to the findings of Armstrong and Niven[2], who have observed that

the deoxyribonucleic acid of several animal viruses has a degree of resistance to deoxyribonuclease.

This staining technique has also been employed for the study of the development of deoxyribonucleic acid in phage-infected *Escherichia coli* and *Bacillus megaterium*, and it has been shown that preparations stained with and without preliminary fixation present a similar picture. Our findings will be described in full at a later date.

Fluorescence microscopy, in combination with methods already in use, may add valuable information both to the study of bacterial cytology and to that of phage development. The simplicity of the technique makes it easy to carry out frequent sampling and the clear-cut difference between ribonucleic and deoxyribonucleic acid fluorescence facilitates rapid determination of the distribution of these two substances.

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[1] Armstrong, J. A., *Exp. Cell. Res.*, **11**, 640 (1956).
[2] Armstrong, J. A., and Niven, J. S. F., *Nature* (previous communication).
[3] Felix, A., and Anderson, E. S., *Nature*, **167**, 603 (1951).
[4] Anderson, E. S., and Felix, A., *J. Gen. Microbiol.*, **9**, 65 (1953).

DISTRIBUTION OF RIBONUCLEIC ACID IN TUMOUR CELLS DURING MITOSIS

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SOME forms of ribonucleic acid are virtually unstained in fixed tissues by dilute solutions of toluidine blue, but can be visualized by subsequent treatment with a molybdate–ferrocyanide solution[1]. Further investigation has shown that ferrocyanide is unnecessary; the staining of various sites of ribonucleic acid by the toluidine blue–molybdate method can be altered in a regular manner by extending the time of fixation in fixatives containing formalin. After short fixation in formalin-free fixatives that preserve ribonucleic acid, the same sequence of staining can be achieved by progressive deamination in dilute solutions of nitrous acid. The entire range of ribonucleic acid staining can be demonstrated in mouse ascites tumours (Table 1) as follows: Wet smears are fixed for periods of 5, 10 and 60 min., 24 hr. and 14 days in formol sublimate at 37° C. After treatment with Lugol's iodine and 5 per cent sodium thiosulphate, the slides are stained in a 0·01 per cent solution of toluidine blue (Coleman Bell Co., dye content 66 per cent) in McIlvaine's buffer at *p*H 3·0 for 30 min., washed for 10 sec. in tap water, and placed in a 5 per cent solution of ammonium molybdate for 30 min. (The effects of fixation or deamination may be simulated to some extent by increasing the concentration of dye or of molybdate. When toluidine blue samples of high dye content are used, lower concentrations of dye or molybdate, or both, may be required to demonstrate all types of ribonucleic acid by this method.) The smears are then rinsed for 10 sec. in running water and dehydrated in tertiary butyl alcohol, cleared in xylol and mounted in 'Permount'. Paraffin sections (10μ thick) prepared from small blocks of tissue from the solid Krebs mouse tumour, sarcoma 180, and from HeLa tumours grown in irradiated rats[3] can be stained in the same fashion. The tissues are fixed for one hour in formol sublimate at 20° C. and the sections are mordanted in formol sublimate at 37° C. as described.

The cells do not stain at all after extraction of nucleic acids with hot trichloracetic acid[3]. Only minimal staining of deoxyribonucleic acid remains when the slides are exposed to 0·1 per cent aqueous ribonuclease for 2 hr. at 37° C. prior to staining.

In cells of the Krebs ascites tumour, ribonucleic acid is stained as shown in Table 1.

Stage I (Fig. 1,*a*,*b*,*c*). Ribonucleic acid is coloured uniformly green in the cytoplasm (diffuse cytoplasmic ribonucleic acid) and blue-green in the nucleolus. The nucleolus decreases in size during prophase, at the end of which nucleolar fragments are sometimes released into the cytoplasm, where they rapidly disintegrate[1]. Finely granular and diffuse parachromatin[1] in the interphase nucleus is stained purple. During prophase large parachromatin bodies are formed, and an increased amount of ill-defined metachromatic material (diffuse parachromatin) accumulates between the chromosomes. In metaphase, this metachromatic material surrounds the pale green chromosomes, while the parachromatin bodies are scattered throughout the cytoplasm (Fig. 1*b*). Some of the diffuse parachromatin is carried over with the chromosomes into the telophase nucleus, but most of it, together with all the parachromatin bodies, persists in the cytoplasm; the parachromatin loses its affinity for stain during the last stages of telophase.

Stage II (Fig. 1,*d*,*e*,*f*). The diffuse cytoplasmic ribonucleic acid and the nucleolus are stained pale green and the intranuclear parachromatin is less intensely stained. The parachromatin granules in

Table 1. Sequence of Staining of Ribonucleic Acid by the Toluidine Blue–Molybdate Method in the Krebs Mouse Ascites Tumour

Stage	Diffuse cytoplasmic ribonucleic acid	Nucleolus	Parachromatin	Cytoplasmic granular and perichromosomal ribonucleic acid	Average fixation time (formol sublimate 37° C.)
I	*G*++	*BG*++	*P*++	—	5–10 min.
II	*G*+	*G*+	*P*+ to *G*+	*P*++	1–24 hr.
III	*P*+++	*BP*++	—*	—	24 hr.–14 days

G, green; *B*, blue; *P*, purple; + to +++ indicates intensity of staining; —, not recognizably stained; *, the larger parachromatin bodies may be faintly stained green

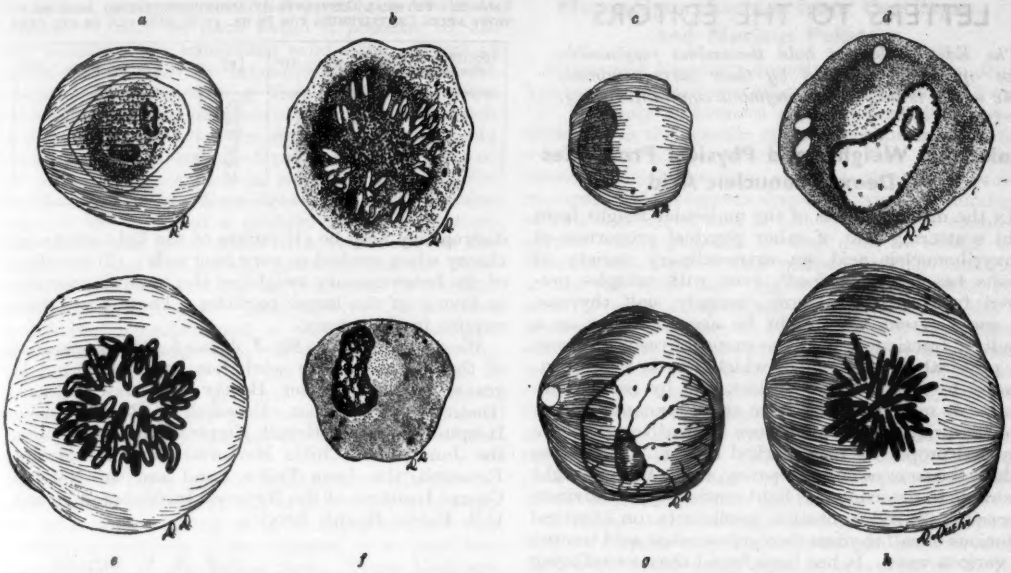

Fig. 1. *a*, Stage I, interphase: green cytoplasm, blue-green nucleolus and finely granular and diffuse purple parachromatin in the nucleus. *b*, Stage I, metaphase: diffuse purple parachromatin around the pale green chromosomes. Large parachromatin bodies in the light green cytoplasm. *c*, Stage I, telophase: finely granular purple parachromatin in the nucleus and parachromatin bodies in the pale green cytoplasm. *d*, Stage II, interphase: purple granular cytoplasmic ribonucleic acid and ill-defined perichromosomal ribonucleic acid. Light green nucleolus and cytoplasm. Pale-staining juxta-nuclear Golgi zone. The vacuoles are caused by lipid globules that have been removed by xylol. *e*, Stage II, metaphase: the chromosomes are surrounded by a well-defined metachromatic sheath which sometimes completely obscures the weakly staining central filament. No granular ribonucleic acid in the pale green cytoplasm. *f*, Stage II, telophase: large parachromatin bodies and finely granular cytoplasmic ribonucleic acid in the light green cytoplasm. Metachromatic perichromosomal ribonucleic acid. *g*, Stage III, interphase: diffuse purple cytoplasm and dark bluish-purple nucleolus. The chromatin (deoxyribonucleic acid) is weakly stained. *h*, Stage III, telophase: diffuse purple cytoplasm, slightly paler than that of the interphase cell. Bluish-purple thin chromosomes

the cytoplasm, especially in the later stages of mitosis, are still intensely stained (Fig. 1*f*). Innumerable minute granules of ribonucleic acid in the cytoplasm (cytoplasmic granular ribonucleic acid) and a diffusely staining form associated with the chromatin (perichromosomal ribonucleic acid) are stained metachromatically in the interphase cell (Fig. 1*d*). During prophase the cytoplasmic granular ribonucleic acid diminishes and the metachromatic ribonucleic acid around the chromosomes increases until, at metaphase, practically all the cytoplasmic granular ribonucleic acid is condensed to form a well-defined sheath around the chromosomes (Fig. 1*e*). This sheath is carried with the chromosomes into the telophase nucleus, where it is gradually replaced by the less well-defined perichromosomal ribonucleic acid of the interphase nucleus. The parachromatin bodies gradually become smaller in the cytoplasm during late telophase and may help to form the cytoplasmic granular ribonucleic acid which reappears at this time.

Stage III (Fig. 1*g* and *h*). After further fixation, the diffuse cytoplasmic ribonucleic acid and, to a lesser extent, the nucleolus stain metachromatically. The diffuse cytoplasmic ribonucleic acid differs from the granular form, which can no longer be recognized, in that it is practically unaltered during the mitotic cycle. The perichromosomal ribonucleic acid, which appears to be related to the cytoplasmic granular form, and all types of parachromatin are not stained.

The larger parachromatin bodies can be coloured faintly by more concentrated solutions of toluidine blue (without the use of molybdate), and, after brief fixation, they may also be demonstrated by various stains for amino-acids[1]. Deamination appears to liberate, from ribonucleoprotein, phosphate groups which bind toluidine blue. At a certain stage of deamination the amount and type of binding of toluidine blue is such that it is capable of reacting with molybdate to produce metachromatic staining.

In summary, an interchange of some forms of ribonucleic acid between the nucleus and cytoplasm appears to take place during mitosis. Nucleolar remnants are sometimes released into the cytoplasm at the onset of metaphase. The parachromatin of the nucleus is extruded into the cytoplasm at the end of prophase and may give rise to the cytoplasmic granular ribonucleic acid of the succeeding interphase. The granular ribonucleic acid that is stained in the cytoplasm of the interphase cell surrounds the chromosomes during prophase and metaphase and contributes to the ribonucleic acid content of the succeeding interphase nucleus. The diffusely staining cytoplasmic ribonucleic acid is altered little, possibly only by dilution during the increase in cell volume associated with mitosis. These observations are consistent with the theory, derived from biochemical studies[4], that there are two classes of ribonucleic acid in the cell: gene-dependent ribonucleic acid in the nucleus and in the cytoplasm, and gene-independent ribonucleic acid in the cytoplasm.

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[1] Love, R., *J. Biophys. and Biochem. Cytol.*, **3**, 123 (1957).
[2] Love, R., Suskind, R. G., and Huebner, R. J., *J. Nat. Cancer Inst.*, **19**, 49 (1957).
[3] Schneider, W. C., *J. Biol. Chem.*, **161**, 293 (1945).
[4] Potter, V. R., *Texas Rep. Biol. and Med.*, **15**, 127 (1957).

LETTERS TO THE EDITORS

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Molecular Weights and Physical Properties of Deoxyribonucleic Acid

In the measurements of the molecular weight from light scattering and of other physical properties of deoxyribonucleic acid, an extraordinary variety of results has been obtained[1], even with samples prepared from a single source, namely, calf thymus. To some extent this might be accounted for as a result of fractionation of the material resulting from its physical heterogeneity, which has been demonstrated by Shooter and Butler[2], and by Schachman *et al.*[3]. It may also arise from small amounts of protein impurity, which have been shown[4] to affect the physical properties to a marked extent. In order to reduce the sources of discrepancy, it has been thought desirable to determine (1) light scattering, (2) intrinsic viscosity, (3) sedimentation coefficients, on identical solutions of calf thymus deoxyribonucleic acid treated in various ways. It has been found that centrifuging as a means of clarifying the solutions is made much more effective by reducing the concentration from 0·1 to 0·04 per cent. Table 1 shows the effect of centrifuging for 18 hr. at 20,000*g* at these two concentrations. The difference must be due to the greater viscosity of the stronger solution. The light-scattering molecular weight, especially of the more turbid samples, is markedly reduced by centrifuging in this way at the lower concentration, without any great change of either the intrinsic viscosity or of the sedimentation coefficients. This must mean that the component which gives rise to high turbidities in the unclarified solutions does not contribute appreciably to the viscosity and sedimentation coefficient. That the high turbidities of the unclarified solutions is not due to deoxyribonucleic acid has been demonstrated by the fact that the action of deoxyribonuclease on a clarified solution (*J*40) with molecular weight 4×10^6 reduced the light scattering to 20 per cent of its original value; while on a turbid solution (*J*38), having an apparent molecular weight of 17×10^6, the light scattering value was reduced by only 40 per cent, that is, to 10×10^6.

The results obtained with a number of preparations when treated in this way now agree very well with each other in most cases (Table 2), and in the exception (*J*38) it has been shown that the high value is not due to deoxyribonucleic acid itself. It will be seen, however, that the molecular weight determined from light scattering in the final solutions is less by a factor of 3 than that determined from the intrinsic viscosity and mean sedimentation coefficient by the equation of Mandelkern *et al.*[5]. The cause of this discrepancy may be (1) failure of the light scattering theory when applied to very long rods; (2) the effect of the heterogeneity weighting the intrinsic viscosity in favour of the larger particles. These possibilities require further study.

Table 1. Effect of Centrifuging Deoxyribonucleic Acid Solutions for 18 hr. at 20,000*g* at Different Concentrations

Sample	Concentration (per cent)	Yield of deoxyribonucleic acid supernatant	$M_L \times 10^6$	$[\eta]$	S_0
J 31 *C*	0·1	88	>20	35	27
	0·04	66	3·0	35	27
J 34	0·1	92	12·2	34	25
	0·04	61	3·3	34	25

Table 2. Physical Constants of Deoxyribonucleic Acid Solutions after Centrifuging for 18 hr. at 20,000*g* at 0·04 per cent

Specimen of deoxyribonucleic acid	$M_L \times 10^6$	$[\eta]$	S_0	$M_{S,\eta} \times 10^6$
31*C*	3·0	35	27	10
33	3·3	29	25	8·5
36	3·3	33·4	28	10·8
40	4·0	50	22	9·0
34	3·3	34	25	9·0
38	17	47	23	9·5

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[1] Reichmann, M. E., Rice, S. A., Thomas, C. A., and Doty, P., *J. Amer. Chem. Soc.*, **76**, 3047 (1954). Sadron, C., Rep. 3rd Int. Cong. Biochem. (Brussels), 210 (1955). Brown, G. L., McEwen, M. B., and Pratt, M. I., *Nature*, **176**, 161 (1955).
[2] Shooter, K. V., and Butler, J. A. V., *Trans. Farad. Soc.*, **52**, 734 (1956).
[3] Schumaker, V. N., and Schachman, H. K., *Biochim. Biophys. Acta*, **23**, 628 (1957).
[4] Butler, J. A. V., Phillips, D. M. P., and Shooter, K. V., *Arch. Biochem.* (in the press).
[5] Mandelkern, L., Krigbaum, W. R., Scheraga, H. A., and Flory, P. J., *J. Chem. Phys.*, **20**, 1392 (1952).

Optical Rotation and Infra-Red Spectra of some Polypeptide and Protein Films

It is well known that the α-helix configuration of Pauling and Corey[1] is associated with a carbonyl stretching mode in the neighbourhood of 1,652–1,655 cm.$^{-1}$ in films of simple enantiomorphic polypeptides[2,3]. Since this frequency is also found in the infra-red spectra of films prepared from a number of native proteins[4–6] it is of interest to know whether other configurations besides the α-helix are associated with it, for some X-ray diffraction photographs of fibrous proteins suggest a mixture of crystalline and amorphous forms. In the case of water-soluble films of *Bombyx mori* silk fibroin[7], a completely amorphous X-ray diffraction pattern can be obtained, along with a carbonyl band in the infra-red spectrum at 1,660 cm.$^{-1}$. It is difficult to think that an α-helix arrangement would not produce sufficient order to reveal the characteristic intensity diffraction pattern of this helix.

The dispersion of optical rotation has recently been shown to be a very useful method for investigating

the helical configuration of polypeptide molecules in solution[8-10], and we have found it possible to use this technique for examining solid films. Films of poly-L-alanine show the anomalous dispersion of the α-helix. It is interesting that Moffitt's b_0 term (which indicates the presence of anomalous dispersion of optical rotation) has the same negative sign and about the same magnitude for poly-L-alanine films as for other L-polypeptides in solution, although the specific rotation in sodium light has a large negative value in the film and a positive value in solution. This shows the great effect of environment on the magnitude and sign of the rotation, and the comparative invariance of b_0, as predicted by Moffitt. Poly-L-tyrosine, however, has a positive b_0 in solution in dimethylformamide and in pyridine; its sodium salt has also a positive b_0 (in film and in aqueous solution). We believe that the unusual sign of b_0 is a consequence of the presence of a strong chromophoric group near the β-carbon, so placed that it must to a great extent share the helical form of the core.

In films of water-soluble *Bombyx mori* silk fibroin, lysozyme and the sodium salt of poly-L-glutamic acid, the value of b_0 is so low as to be negligible, and this is taken as evidence of the absence, or at least low concentration, of the helical form. These films are not in the extended β-configuration however (as shown by the absence of a carbonyl band at 1,630 cm.$^{-1}$). The silk films, even after intensive drying, show no peak in the spectrum at 3,460 cm.$^{-1}$ (the 'free' NH stretching mode), and it must be concluded that substantially all the peptide hydrogen bands are formed, in what appears to be a disordered state.

It is clear from these observations that a carbonyl band at about 1,660 cm.$^{-1}$ is observed in polypeptide spectra not only with the α-helix and collagen folds[6,11] but also in what, in the absence of further evidence, seems to be a disordered state. In the case of some globular proteins, a certain amount of order presumably persists in solid films, but in lysozyme it is not of a kind which gives rise to anomalous dispersion of optical rotation. These results contrast with those found by Cohen and Szent-Gyorgi[12] in muscle proteins, where in aqueous solution the α-helix configuration appears to be dominant.

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[1] Pauling, L., and Corey, R. B., *Proc. U.S. Nat. Acad. Sci.*, **37**, 235 (1951).
[2] Ambrose, E. J., and Elliott, A., *Proc. Roy. Soc.*, A, **205**, 47 (1951).
[3] Elliott, A., *Proc. Roy. Soc.*, A, **221**, 104 (1953).
[4] Ambrose, E. J., and Elliott, A., *Proc. Roy. Soc.*, A, **208**, 75 (1951).
[5] Rudall, K. M., "Adv. in Protein Chem.", **7**, 253 (1952).
[6] Ambrose, E. J., and Elliott, A., *Proc. Roy. Soc.*, A, **206**, 206 (1951).
[7] Ambrose, E. J., Bamford, C. H., Elliott, A., and Hanby, W. E., *Nature*, **167**, 264 (1951).
[8] Yang, J. T., and Doty, P., *J. Amer. Chem. Soc.*, **79**, 761 (1957).
[9] Moffitt, W., *Proc. U.S. Nat. Acad. Sci.*, **42**, 736 (1956).
[10] Moffitt, W., and Yang, J. T., *Proc. U.S. Nat. Acad. Sci.*, **42**, 596 (1956).
[11] Fraser, R. B. D., *Disc. Farad. Soc.*, No. 9, 378 (1950).
[12] Cohen, C., and Szent-Györgi, A. G., *J. Amer. Chem. Soc.*, **79**, 248 (1957).

Mucopolysaccharides from Cartilage and Nucleus Pulposus

Meyer and Rapport[1] described the isolation from hyaline cartilage of two chondroitin sulphates, *A* and *C*. The only differences so far reported[2] between these are in the specific optical rotation and alcohol solubility of their calcium salts. Orr[3] found that chondroitin sulphate from cartilage gives an infra-red spectrum which suggests that the product is a mixture of two isomers, *A* and *B* (see below). By countercurrent electrophoresis he was able to obtain the faster component of this mixture, which exhibited in the 700–1,000 cm.$^{-1}$ region 3 bands, at 928, 855 and 725 cm.$^{-1}$, respectively, and was called the *A* isomer. The *B* isomer, on the other hand, was isolated alone in a well-defined form from the nucleus pulposus and showed two bands at 825 and 775 cm.$^{-1}$, respectively. Meyer *et al.*[2] pointed out the similarity between Orr's *B* isomer and chondroitin sulphate *C*. On the other hand, both *A* types show the same optical rotation and origin. The following results seem to give a different picture of the mucopolysaccharides of cartilage and nucleus pulposus.

Extracts of (*a*) cartilage from horse nasal septum and (*b*) nucleus pulposus from human intervertebral disk were made using aqueous solutions of 30 per cent potassium chloride and 1 per cent potassium carbonate[4].

These were centrifuged, and the resulting solutions were dialysed. The retained soluble fractions were then precipitated with potassium acetate and alcohol at 0° C. The precipitates so obtained were purified by application of this technique three times; finally, the resulting specimens were dried with absolute alcohol and ether.

A preliminary paper electrophoresis of our preparations *MC* (from cartilage) and *MP* (from nucleus pulposus) showed the same main features, that is, two components were present and both stained metachromatically with toluidine blue. One component was stationary and the second one mobile and negatively charged. A previous investigation[5] showed that in *MC* the first component was mucoprotein, the second one being chondroitin sulphate. By analogy, the immobile component of *MP* was thought to be a protein–polysaccharide complex, the mobile one a mucopolysaccharide. The amino-acid composition of *MP* was shown, by paper chromatography, to be similar to that of *MC*, already reported elsewhere[5].

An infra-red investigation gave the following results. Both *MC* and *MP* showed the spectrum of Orr's *A* isomer. *MC* was repeatedly treated with kieselguhr to give a mucopolysaccharide free from mucoprotein which showed an *A*-type spectrum (Fig. 1). The same infra-red spectrum was obtained from a crystalline calcium chrondroitin sulphate[6] (which is a mixture of chondroitin sulphates *A* and *C*, following Meyer's criteria), and a preparation obtained by deproteinizing a mucoprotein from cartilage[7]. Therefore, we suggest that only one type of chondroitin sulphate is present in cartilage. This appears to confirm Meyer's hypothesis[2] that chondroitin sulphates *A* and *C* are only two fractions of the same polydisperse substance.

By treatment of *MP* with kieselguhr we obtained a free mucopolysaccharide which showed the *B* isomer spectrum (Fig. 2). Using paper chromatography and analytical methods, this mucopoly-

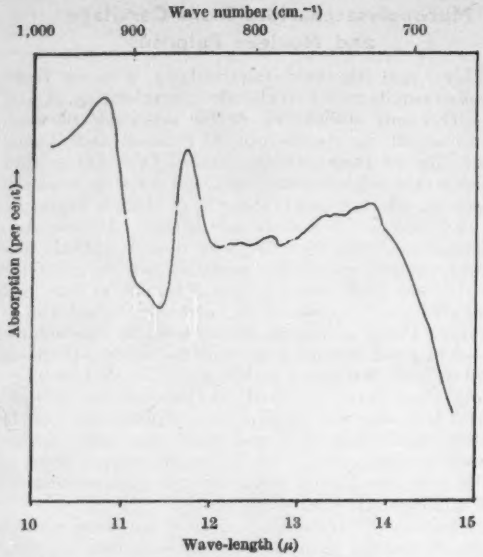

Fig. 1. Infra-red spectrum of chondroitin sulphate

saccharide was identified as keratosulphate (in agreement with a previous finding on a similar preparation[8]). It is reasonable to conclude, therefore, that *MP* is a mixture of a mucoprotein the carbohydrate component of which is chondroitin sulphate and a free mucopolysaccharide, keratosulphate. We cannot, however, exclude the presence as minor constituents of keratosulphate in mucoprotein or of chondroitin sulphate in the mobile component of *MP*. The lower intensity of the 1,736 cm.$^{-1}$ band in comparison with that at 1,560 cm.$^{-1}$ found by Orr in the *B* type as compared to the *A* type (attributed by him to a lower hexuronic acid : hexosamine ratio) is in agreement with our conclusions.

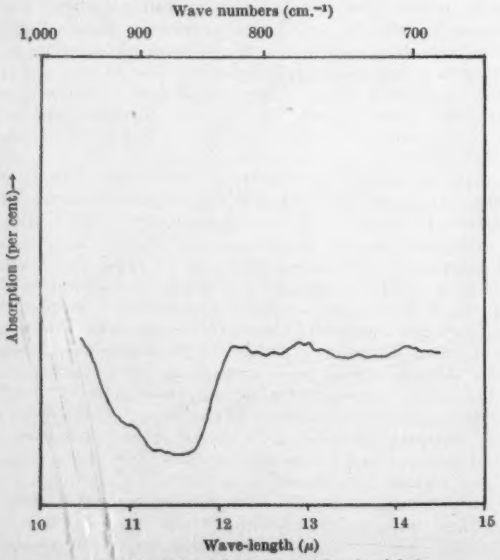

Fig. 2. Infra-red spectrum of keratosulphate

A more detailed presentation of this work will be given elsewhere in due course.

We are indebted to Prof. M. Schubert for the generous gift of samples of crystalline calcium chondroitin sulphate and mucoprotein, and to our colleague Mr. J. H. Keighley for valuable assistance in the infra-red investigations. One of us (G. B.) thanks the Bradford Education Authority and the Bradford Group *A* Hospital Management Committee for a joint scholarship to carry out this work.

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[1] Meyer, K., and Rapport, M. M., *Science*, **113**, 596 (1951).
[2] Meyer, K., Davidson, E., Linker, A., and Hoffman, P., *Biochim. Biophys. Acta*, **21**, 506 (1956).
[3] Orr, S. F. D., *Biochim. Biophys. Acta*, **14**, 173 (1954).
[4] Einbinder, J., and Schubert, M., *J. Biol. Chem.*, **185**, 725 (1950).
[5] Bernardi, G., Cessi, C., and Gotte, L., *Experientia* (in the press).
[6] Einbinder, J., and Schubert, M., *J. Biol. Chem.*, **191**, 591 (1951).
[7] Shatton, J., and Schubert, M., *J. Biol. Chem.*, **211**, 565 (1954).
[8] Hall, D. A., Lloyd, P. F., Happey, F., Horton, W. G., and Naylor, A., *Nature*, **179**, 1078 (1957).

Excitation of Molecular Spectra by Shock Waves

Several spectroscopic studies have recently been made of the light emitted from gases submitted to an intense shock wave[1–3], but little information is available about the emission from air and other permanent gases. The very high temperatures available make the shock tube a convenient device for study of spectra of astrophysical interest, and a knowledge of the spectrum of air is necessary in any consideration of its high-temperature emissivity which may be required for problems of supersonic flight at high altitude. We have studied emission from air, nitrogen, oxygen, carbon monoxide and carbon dioxide or mixtures of these with argon.

The shock tube, 5 ft. long and 2½ in. in diameter, is of copper, as this has a simple spectrum which does not interfere with that of the gas being studied. The emission was studied through quartz side-windows. For examination of the primary shock wave, a dump chamber was used for preventing its reflexion, while for the hotter reflected shock an end-plug was inserted close to the windows. Other features were similar to those used by Fairbairn and Gaydon[3]. Spectra were recorded photographically with a small *f*/4 'Hilger' Raman spectrograph. Comparison of the variation in time of light emission of two spectrum lines was made by using two spectrometers set to view the same point of the shock from opposite sides; the spectrometers were fitted with photomultipliers, connected to a 'Cossor' 1038 double-beam oscillograph.

Strong reflected shocks through pure argon (99·8 per cent) give intense light emission[1], the spectrum showing argon lines superposed on a continuum

Fig. 1 (*a*). Spectrum of a reflected shock through argon + hydrogen, showing Balmer and argon lines. Primary shock Mach No. 5·9. Neon comparison spectrum

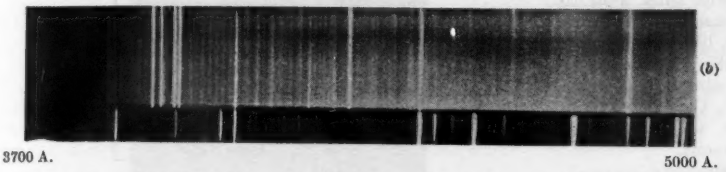

Fig. 1 (*b*). Shock through argon + oxygen, showing structure of Schumann–Runge bands. Neon comparison spectrum

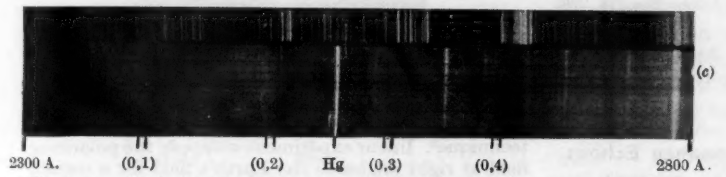

Fig. 1 (*c*). Shock through argon + air, showing NO γ-bands. Iron-arc comparison spectrum. Primary shock Mach No. 8·3

with a number of impurity lines, including the Balmer lines of H, lines of Hg, Na, Ca, Ca+ and K, and strong CN-bands. We attribute the hydrogen emission to residual molecular hydrogen in the tube and not, as has previously been suggested, to interaction of the hot gases of the reflected shock with the hydrogen driver-gas. Photo-electric records show H_β emission at the same instant as light in the region of the argon lines and the mercury lines. Addition of hydrogen to the argon strengthens the Balmer lines, H_α, H_β, H_γ and H_δ. As the intensity of the shock wave is increased, these lines broaden (Fig. 1*a*), H_γ and H_δ eventually becoming so broad as to be indistinguishable from the general continuum. The calculated temperature is about 12,000° K., and the breadth of the Balmer lines is consistent with this. The CN-violet bands appear to show very high rotational and vibrational temperatures, the 'tail bands' (15,15) to (11,11) being strong. The emission from a primary shock wave through argon is weak, but, at a calculated temperature of 6,000° K., we have photographed the spectrum using a wide slit, obtaining lines of Na, Ca and Ca+ and bands of CaO or CaOH on a continuous background. Simultaneous comparison of the sodium or calcium light emission with that of the continuum shows a significant delay of up to 30 μsec. for the former. The continuous radiation produces a small initial pulse, with a sharp leading edge; this decays for about 30 μsec., and then rises relatively slowly, before it is suddenly quenched by the contact surface. Pulses recording the sodium *D*-line, Ca 4226 A., and Ca+ 3933 A. and 3968 A. lines are much stronger (× 500), but occur later and correspond to the slow rise of the continuous radiation pulse. The leading pulse is attributed to rotational structure from C_2 bands. The main sodium, calcium, etc., emission and the slow rise in continuous emission are attributed to impurities scrubbed from the walls and drawn later into the hot gases. These alkali and alkaline earths cannot exist initially in the gas phase, and much of the luminosity, and possibly of the ionization, observed behind moderate shocks is due to impurities brought from the walls in this way; in steel tubes, lines of Fe and bands of FeO will be produced. This effect could give rise to the impression of a delay between the passage of a shock front and the onset of luminosity.

Shocks through oxygen show the Schumann–Runge bands of O_2. This has been reported previously[3]; but, with these clearer spectra, the structure is more evident and extends to 4300 A. (see Fig. 1*b*). Nitrogen/argon mixtures show the Second Positive system of N_2 and the First Negative system of N_2+. Rose[4] suggested that the First Positive system was present, but we have not observed them on our plates. There is a good deal of continuum towards the red, and the bands of the red system of CN, as well as the violet system, occur as impurity.

Relatively mild shocks through argon/air show the Schumann–Runge bands of O_2 strongly, with about the same intensity as in pure oxygen. As the temperature is raised by increasing the strength of the shock, the N_2 Second Positive, N_2+, CN-violet and CN-red, all superposed on the Schumann–Runge, are the most prominent features between 3000 and 7000 A. The 3360-A. band of NH, and the 2811 and 3064-A. bands of OH also occur. Below 3000 A., the NO system is prominent; this, contrary to Rose's anticipation[4], shows sharp heads and clearly resolved structure (Fig. 1*c*) with a high rotational temperature. We have not, however, observed any bands of the β-system of NO. The yellow-green continuum, due to association between NO and atomic oxygen (namely, air afterglow), is not observed; presumably the probability of the association, $NO + O = NO_2 + h\nu$, is too small to give much light in the short time available. In laboratory experiments, the CN-red bands in the near infra-red would probably contribute appreciably to the emissivity of air, although they might be absent from clean air.

As previously reported[3], both CO and CO_2 give very strong Swan bands of C_2. We have now observed CH from CO containing H_2 or H_2O (supporting formation of CH from C_2 + OH) and, in very hot shocks through CO, we have detected the Mulliken band of C_2 near 2325 A.; the C line at 2478 A. is strong and some bands of the Fourth Positive system of CO are visible. We have not observed either the strong Ångström or Third Positive systems of CO. The C_2 high-pressure bands, which might indicate formation of C_2 via a carbon-atom association process, are absent.

The spectra excited by shock waves are thus very different from those obtained by electrical discharges through similar mixtures. The Schumann–Runge bands, for example, occur in shock waves, but not in ordinary discharges, while the N_2 First Positive and the CO Third Positive and Ångström bands, which are such strong features of Geissler tube spectra, do not occur. In discharges, excitation is due mainly to electron impact, whereas molecular collisions are probably more important in the thermal excitation in shock waves. Shock tube spectra thus tend to resemble those excited in King furnaces. Temperatures in King furnaces are, however, limited to below about 3,000° C., whereas shock tubes enable us to reach temperatures nearer those of stellar sources.

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[1] Resler, E. L., Lin, S.-C., and Kantrowitz, A., *J. App. Phys.*, **23**, 1390 (1952).
[2] Greene, E. F., *J. Amer. Chem. Soc.*, **76**, 2127 (1954).
[3] Fairbairn, A. R., and Gaydon, A. G., *Proc. Roy. Soc.*, A, **239**, 464 (1957).
[4] Rose, P. H., Avco Res. Lab. Res. Note, No. 37 (May 1957).

Audio-frequency Nuclear-resonance Echoes

The principal expense and source of difficulty in equipment for nuclear magnetic resonance is the magnet to provide the large magnetic field. It has been shown that a nuclear-resonance signal can be obtained using only the Earth's field[1,2]. This is the so-called free-precession experiment, in which the nuclear system is first polarized at right angles to the Earth's field by means of a simple current-carrying coil. After removal of this field, the nuclear magnetization precesses about the Earth's field (approximately 0·48 gauss) and induces an alternating voltage in the same coil at a frequency of about 2 kc./s., which may be observed after suitable amplification. The polarizing field serves the double purpose of producing a nuclear magnetization appropriate to a large field and hence a stronger signal to be observed in the smaller field, and also produces this polarization at right angles to the small field. The signal is attenuated by loss of phase-coherence of the precessing nuclei, due both to interactions between them with a time constant T_2, and to inhomogeneity in the Earth's field (T_2^*). The method can be used for measuring the decay time, T_2, which is a property of the material, by observing the decay of the precession signal, provided the inhomogeneity of the Earth's field is sufficiently small for $T_2^* \gg T_2$. In many cases, for example, in liquids such as water containing mobile protons, T_2 may be several seconds and the corresponding field inhomogeneity must be less than 10 microgauss/cm. in order to measure T_2. This implies that the experiment cannot be performed in the laboratory and usually requires the sample coil to be placed out of doors away from all buildings (we have found a brick wall to be unacceptably magnetic in this sense).

In order to avoid this difficulty and to make it possible to carry out measurements in the laboratory without undue precautions and indeed to measure time-constants of such length that requirements of homogeneity would be excessive, we have devised a method

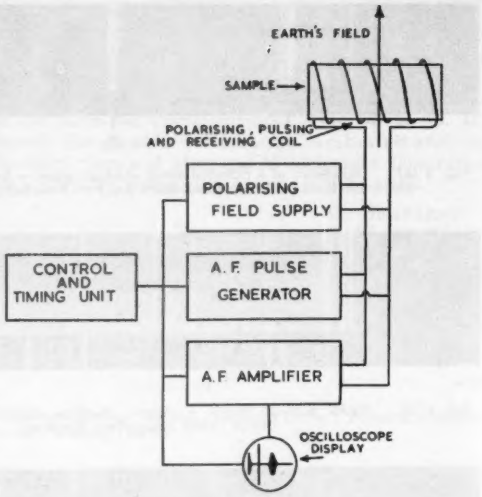

Fig. 1

of measurement which circumvents the difficulty due to the field inhomogeneity in a manner similar to that used at higher fields, namely, by a spin-echo technique[3]. In our experiment we apply the polarizing field at right angles to the Earth's field for a certain time, T, longer than T_1 and then remove it (Fig. 1). In passing, we note that a free-precession signal is observed (Fig. 2) which is attenuated by field in-

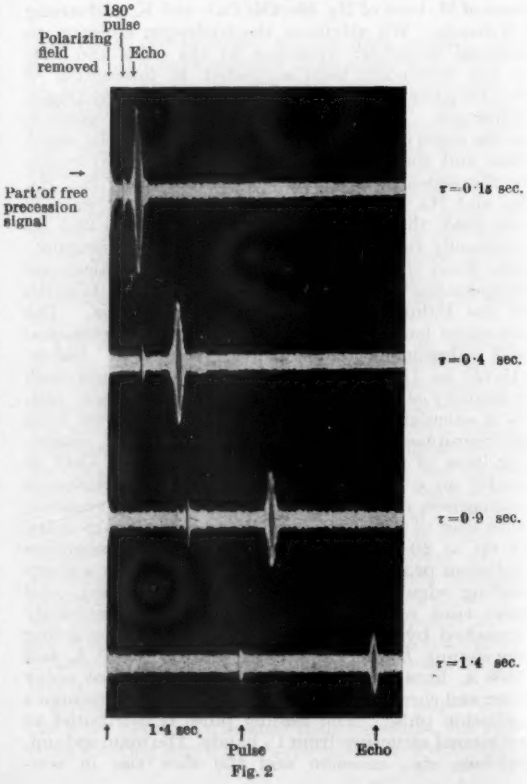

Fig. 2

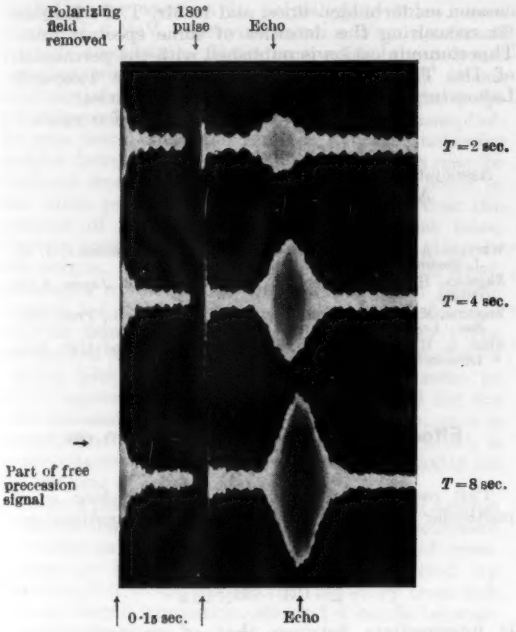

Fig. 3

homogeneities (75 microgauss/cm.). At a time τ later, we apply a '180°-pulse' at the resonant frequency in the Earth's field (actually 2 kc./s., 20 msec. and 0·1 V.). At a further time τ later, the echo pulse is observed on the oscilloscope. The width of the echo is inversely proportional to the field inhomogeneity. By varying the time τ, the delay of the pulse after the removal of the polarizing field, we observe echoes the amplitude of which is proportional to $\exp(-2\tau/T_2)$ This effect is shown in Fig. 2. We are thus able to derive a value of T_2 the true spin – spin relaxation time in the presence of field inhomogeneity just as in the echo experiment at high fields. We have also the advantage, usual in echo measurements, of observing our signals (a few microvolts) at times well removed from disturbing effects due to polarizing and pulse voltages. In the example shown the sample was double-distilled water, and we find $T_2 = 3{\cdot}5$ sec. which is the expected value, since T_1 at low fields is 3·5 sec [4] and we should have $T_1 = T_2$ in this case.

The free-precession experiment has also been used to measure T_1 the spin – lattice relaxation time in low fields[2,5]. In this experiment the amplitude of the free-precession signal is observed as a function of the time of application of the polarizing field, T, and is proportional to $\{1 - \exp(-T/T_1)\}$. This method suffers from the same difficulty as the precession method for T_2, but in less acute form, since it involves observing a free-precession signal immediately after switching off a large current in the coil with its attendant transients. Our method considerably simplifies this problem also, in that we again apply a '180°-pulse' but always at a fixed time, τ', after switching off the polarizing field and observe the amplitude of the echo—which should be proportional to $\{1 - \exp(-T/T_1)\}$—as a function of T. The effect is shown in Fig. 3. The derived value of T_1 in this case is 3·5 sec., and this is the value of T_1 for a field of 200 gauss (the polarizing field), which agrees with previous measurements[2] as well as with our value of T_2 as already mentioned.

In the experiments described a sample of 500 ml. of water was used, but we hope to be able to reduce this considerably in due course, since almost all the noise now observed is extraneous pick-up and it should be possible to shield it, albeit with difficulty.

We intend to use this method for measuring T_1 and T_2 and self-diffusion coefficients of liquids. For this purpose the apparatus is extremely cheap and simple, and there is, of course, the added interest of being able to measure the parameters T_1 and T_2 at low fields for materials in which they differ from the high-field values.

Note added in proof: We now get the same signal-to-noise ratio from a 100-ml. sample.

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[1] Packard, M., and Varian, R., *Phys. Rev.*, **93**, 941 (1954).
[2] Waters, G. S., and Phillips, G., *Geophysical Prospecting*, **4**, No. 1 (1956).
[3] Hahn, E. L., *Phys. Rev.*, **80**, 580 (1950).
[4] Giulotto, L., *Arch. Sci.*, **9**, Report of 5th Colloque AMPERE, p. 218 (1956).
[5] Waters, G. S., and Francis, P. D., S.R.D.E. Report No. 1097 (Ministry of Supply, Oct. 1955).

Multipole Radiation from High-Current Gas Discharges

Research in the field of high-current gas discharges is now being pursued vigorously[1]. In these discharges, where the gas is highly ionized, higher spectra can be predominantly excited (for example, O III, A II) and the pinch effect reduces the loss of ions to the walls. It is thus interesting to consider the possibility of detecting in the laboratory those forbidden lines which are of astrophysical importance.

In the past, very little success has been achieved in this direction. Nagaoka and Futagami[2] claim to have obtained forbidden lines of the N II, N III and O II spectra but not of the O III spectrum. Their paper is unfortunately completely devoid of any detailed spectral data. On the other hand, Emeléus, Sloane and Cathcart[3] were unable to obtain forbidden lines of ionized nitrogen, oxygen and neon in their discharges. The view has also been expressed that it is impossible to produce sufficient numbers of these ions in the requisite metastable levels to build up the intensities of the forbidden lines to observable values[4]. Here it is shown that there is a reasonable chance of detecting some forbidden lines (transition probability greater than 1 sec.$^{-1}$) of highly ionized atoms in the radiation from a high-current discharge using a conventional prism spectrograph of medium aperture.

We estimate the time required to record the forbidden line of a spark spectrum on a photographic plate in the following way. By comparing the exposure times required for the detection of permitted and forbidden lines of the same spectrum, we avoid the difficulty of estimating the population, N, of the metastable levels. The optical density of a spectral line (wave-length λ) on a photographic plate is a function of NAt/λ where A is the spontaneous transition probability and t the exposure time. Let

us denote an optically permitted line by the subscript p and a forbidden line by the subscript f. We assume the ionized gas to be in thermal equilibrium at the temperature T. By applying Boltzmann's distribution law to the two atomic states in question with statistical weights g_p and g_f, and separated by an energy difference E_{pf},

$$t_f = \frac{g_p}{g_f}\,\frac{A_p}{A_f}\,\frac{\lambda_f}{\lambda_p}\exp\left(-\frac{E_{pf}}{kT}\right)\cdot t_p$$

provided that the density of the two lines is the same. Variations in spectral sensitivity and reciprocity failure of the photographic plate are neglected. The time t_f can therefore be estimated from the known exposure time of a permitted line under typical experimental conditions of a pulsed high-current discharge. For example, at a pressure of 3×10^{-3} mm. of mercury in nitrogen gas and an exposure time of 4×10^{-4} sec., the measured density of the permitted line N II λ 3,995·0 recorded with a Hilger prism spectrograph of focal ratio $f/7$ on an *HP*3 plate (by Ilford, Ltd.) was 1·4. Let kT be about 20 eV. and the forbidden line selected for comparison, [N II] λ 5,755. For this line, t_f is computed to be about 1×10^5 sec. This time represents an upper limit and will be less if thermal equilibrium does not exist. If the discharge is run at a reasonable duty cycle (for example, 0·02), it will take from several hours to about one day to produce a perceptible blackening on a photographic plate (for example, density 0·4) for some four forbidden lines of the ionized atoms ofargon, neon and oxygen in addition to [N II] λ 5,755.

In high-current discharges operating at low pressures, thermodynamic equilibrium does not exist, nor is there as yet any conclusive evidence that the electrons and ions are in thermal equilibrium. However, on the basis that the populations of metastable ionized atoms in the ground configuration are governed by Boltzmann's distribution law (cf. the condition of gaseous nebulæ in the limit of high electron concentration), the electron temperature of the discharge can be estimated by measuring the relative intensities of two of the forbidden lines. The method is limited to temperatures up to about 10^5 deg. K. owing to the increasing insensitivity of the exponential factor in the Boltzmann distribution as the temperature rises. It may therefore be of greater value to low-current discharges in, say, the rare gases. Relative values of transition probabilities can possibly be determined, provided either an independent measurement of the electron temperature has been made or it is so high that the exponential factor can be taken as unity. A check could then be made of forbidden transition probabilities of astrophysical interest which have been determined either by calculation or from observations on nebular lines.

I am grateful to Dr. R. H. Garstang, University of London Observatory, for a discussion on forbidden lines, and to Mr. T. P. Hughes for measuring the densities of some spectral lines. This communication is published with the permission of Dr. T. E. Allibone, director of the Research Laboratory, Associated Electrical Industries.

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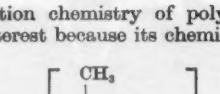
[1] Ware, A. A., *Phil. Trans.*, A, **243**, 197 (1951). Kurchatov, I. V., *J. Nuclear Energy*, **4**, 193 (1957). And others.
[2] Nagaoka, H., and Futagami, T., *Proc. Imp. Acad. Japan*, **8**, 78 (1932).
[3] Emeléus, K. G., Sloane, R. H., and Cathcart, E. B., *Proc. Phys. Soc., Lond.*, **51**, 978 (1939).
[4] Aller, L. H., "Gaseous Nebulae", 166 (Chapman and Hall, Ltd., London, 1956).

Effect of High-Energy Radiation on Polypropylene

The radiation chemistry of polypropylene is of particular interest because its chemical constitution:



is intermediate between that of poly*iso*butylene, which exhibits molecular degradation, and that of polyethylene in which although some degradation occurs, cross-linking predominates. It has been reported in the literature that polypropylene undergoes cross-linking on exposure to high-energy radiation[1], but no information has hitherto been reported as to the extent to which molecular degradation takes place. For this reason we have undertaken an investigation of the radiation chemistry of polypropylene, the preliminary results of which are given below.

A specimen of polypropylene, prepared by the Ziegler process, was made available by courtesy of Montecatini of Milan. The number average molecular weight of the material, determined from the intrinsic viscosity by the method described by Ciampa[2] was found to be of the order of 90,000.

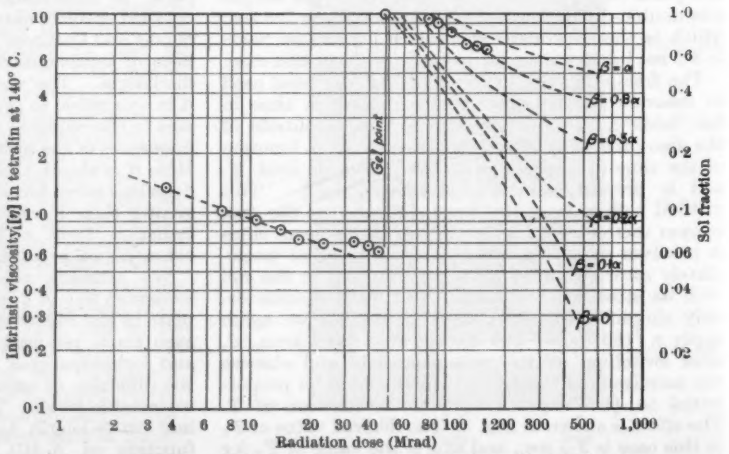


Fig. 1. Variation of intrinsic viscosity and sol fraction with radiation dose

Samples of the polymer were irradiated, while sealed under vacuum in polyethylene tubes, in a beam of 2-MeV. electrons from a Van de Graaff particle accelerator. Doses received by the polymer samples were estimated by carrying out elastic modulus measurements at 150° C. upon the polyethylene tubes which had contained the samples[3]. It was found that the number average molecular weight decreased steadily in a manner which may be deduced from the assumption that breaks occur in the main polymer chain at random, and that the number of breaks produced is, initially at least, directly proportional to the radiation dose given to the sample. After a radiation dose of about 50 Mrad, prolonged extraction of the polymer with boiling toluene led to the separation of a cross-linked gel fraction from the soluble, degraded, polymer. The gel showed appreciable swelling in the toluene and a log–log plot of the equilibrium swelling ratio at 25° C. against the radiation dose, corrected for the dose necessary to bring about gel formation, gave a straight-line relationship of gradient $-5/3$, which is in accordance with the Flory–Rehner relationship for the swelling of cross-linked polymer[4].

From a plot of the values of the sol fraction against radiation dose when compared with the theoretical sol values in the presence of various ratios of cross-linking to molecular degradation as derived by Charlesby[5], it would appear that for every cross-link formed during irradiation, about 1·6 bonds between monomer units are broken.

Fig. 1 shows the variation of the experimental values of the sol fractions with radiation dose; and, in addition, a plot of the intrinsic viscosity of a solution of the polymer up to the gel point.

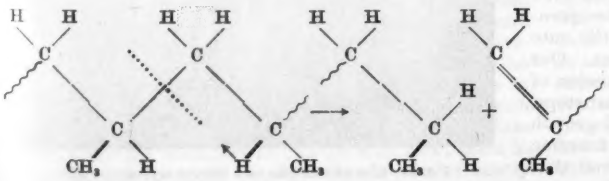
Approximate yields (G values) for an energy deposition of 100 eV. are given in Table 1, which compares the yields with those of polyethylene and poly*iso*butylene.

Table 1

Event	Events per 100 eV. deposition		
	Polyethylene	Poly*iso*butylene	Polypropylene
Cross-links	6·8	0	0·6
Double bonds	3·4	9·3	3·9
Bonds between monomers broken	3·0	5·0	0·9

An examination of the infra-red absorption spectrum of irradiated polypropylene has shown that the principal chemical change, other than cross-linking and chain fracture, is the introduction of unsaturation of the type $R.R'C{=}CH_2$ (vinylidene). There is some evidence for the presence of a small amount of vinyl unsaturation, $RCH{=}CHR'$, but the band is obscured by another absorption band which has not yet been assigned.

It is suggested that the molecular degradation proceeds by the following disproportionation mechanism:



It is hoped to report the results of this investigation more fully at a later stage.

We thank Miss D. E. Bowles for infra-red measurements, and Dr. L. G. Brazier, director of research and education, British Insulated Callender's Cables, Ltd., for permission to publish this communication.

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[1] Miller, A. A., Lawton, E. J., and Balwit, J. S., *J. Poly. Sci.*, **14**, 503 (1954).
[2] Ciampa, G., *La Chimica e l'Industria*, **38**, 298 (1956).
[3] Black, R. M., *Nature*, **178**, 305 (1956).
[4] Flory, P., and Rehner, J., *J. Chem. Phys.*, **11**, 521 (1943).
[5] Charlesby, A., *J. Poly. Sci.*, **11**, 513 (1953).

The Tanberg Effect

In a recent communication, Robson and von Engel[1] have suggested that Tanberg's explanation of the reaction force on the cathode of an arc in vacuum is incorrect, and that the mass used in his momentum equation should have been a hundred times larger, giving rise to a more 'reasonable' particle velocity of 10^4 cm./sec. rather than 10^6 cm./sec.

It is exceedingly difficult to reconcile this suggestion with the results of Easton, Lucas and Creedy[2], who obtained velocities which agreed fairly well with Tanberg's, by a method which did not directly involve the cathode, but measured the force on a vane facing the cathode some two centimetres away from it. Their results were obtained with rather a poor vacuum (40×10^{-3} mm. mercury).

Experiments have been made in these laboratories in which the force exerted on a vane mounted behind a perforated anode by vapour emitted from the cathode of a vacuum arc has been measured. The vacuum was better than 10^{-3} mm. mercury, the metal vapour cast sharp shadows, and the space potential at the vane was measured to be certain that electrostatic effects were not influencing the vane. The average velocity of the vapour jet from a cathode spot on magnesium was found to be about 2×10^5 cm./sec. and from a cathode spot on copper about 1×10^6 cm./sec. These figures agree well with those quoted by Easton, Lucas and Creedy. While the nature of the experiments is such that the results cannot be expected to be highly accurate, there seems no doubt that the orders of magnitude are correct and that vapour is in fact ejected from the neighbourhood of cathode spots in vacuum, although not necessarily from the metal surface, with these high velocities. These results have been discussed with Drs. Robson and von Engel, whose most recent views are expressed in a paper shortly to be published.

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[1] *Nature*, **179**, 625 (1957).
[2] Easton, Lucas and Creedy, *Elect. Eng.*, 1454 (1934).

Growth of Sucrose Crystals

Layer growth on crystals was observed by Marcelin[1] and other workers. Steps on crystals could be produced by surface nucleation or by the presence of screw dislocations which terminate at the surface[2]. The layers on cadmium iodide growing in aqueous solution[3] were shown by Forty[4] to be steps originating from dislocations. While Bunn[5] was unable to find any layers on growing sucrose crystals, Powers[5] observed them but without seeing any definite signs that they were due to screw dislocations. We have made an extensive examination of the surface features of sucrose crystals grown in the temperature-range 15–30° C. and conclude that the normal growth process is that described by Frank[2]. Step systems in the form of growth hills have been shown to be present on all faces of sucrose crystals when grown in pure sucrose solution and in sucrose solution with added dextrose or lævulose as impurity. Crystals grown in sucrose solution with added dextrose (0·2 per cent by weight of the sucrose) have steps which generally are much larger (about 40 times) than those grown in pure solutions of sucrose or in solutions with added lævulose.

Fig. 1. 100-face of growing sucrose crystal showing: 1, simple growth spiral: 2, double spiral (× 60)

A photomicrograph (Fig. 1) was taken of the 100-face of a crystal while still growing. On it can be seen a simple growth spiral centred on a screw dislocation and also a double spiral with centres on a close pair of dislocations of like sign. On other crystals dislocation pairs of opposite sign give rise to closed loops of steps, and the shape of the loops on any one face is essentially constant. The shapes are asymmetric, those on the 100-face being roughly D-shaped, indicating that the edge free energy depends on the orientation. Radial lines are frequently observed on the growth hills and are provisionally ascribed to the interaction of number of growth centres in close proximity.

The rate of movement of the steps, the spacing between them and their heights can be measured under known conditions of supersaturation, temperature and stirring. On any one growth hill the rate of movement of steps is found to be constant. Our results are in broad agreement with the discussion of Burton, Cabrera and Frank[6] for monomolecular steps. From the measurements, the rate of vertical growth of the hill can be derived and is shown as a function of concentration in Fig. 2. It will be observed that

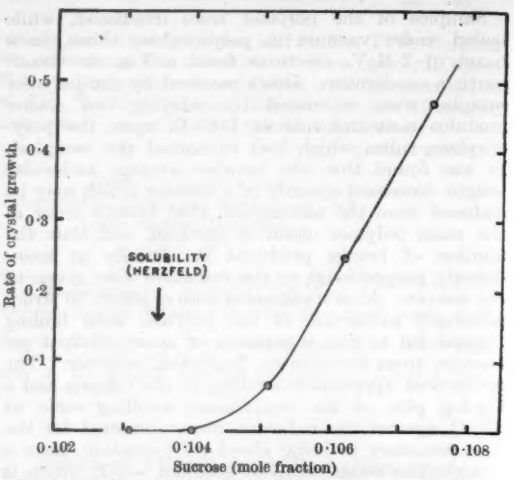

Fig. 2. Relative rate of vertical growth of 100-face as a function of the concentration of the solution

growth ceases at an appreciable supersaturation: this effect has been observed a number of times and is attributed to the distance between dislocation centres being less than the dimension of the critical surface nucleus. Owing to the varying activities of the growth centres, equivalent faces of different crystals show different rates of vertical growth at the same supersaturation. This is in qualitative agreement with the unpublished work of Garner and Wischin, who found variations of up to 50 per cent in the gross rates of growth measured on single sucrose crystals.

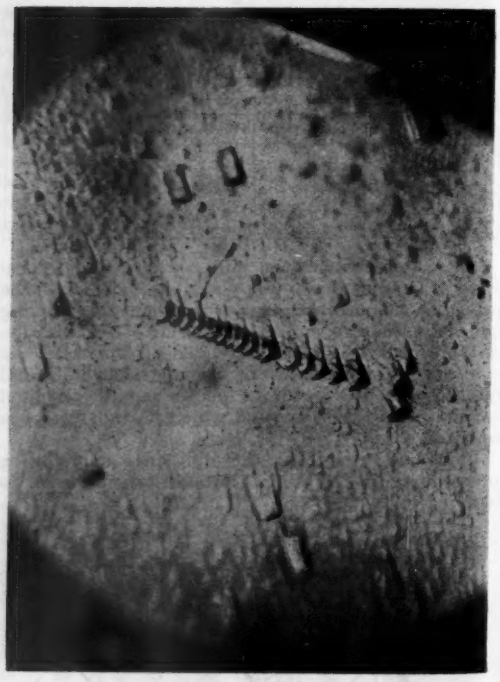

Fig. 3. Line of etch pits on a sucrose crystal (× 400)

On reducing the concentration of the solution to saturation and just below, the first sign of crystal dissolution is the formation of small etch pits at the ends of dislocations where the molecules are less firmly bound than on the rest of the crystal surface[7]. We have studied the formation and distribution of etch pits on sucrose crystals, and the linear arrangement seen in Fig. 3 is not uncommon. The number, position and size of the pits can be related to the conditions under which the crystal was grown.

We wish to thank Mr. H. C. S. de Whalley and the directors of Tate and Lyle, Ltd., for their interest and encouragement.

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[1] Marcelin, A., *Ann. Phys.* **10**, 185 (1918).
[2] Frank, F. C., *Discuss. Farad. Soc.*, **5**, 48 (1949).
[3] Bunn, C. W., *Discuss. Farad. Soc.*, **5**, 132 (1949).
[4] Forty, A. J., *Phil. Mag.*, **43**, 72 (1952).
[5] Powers, H. E. C., *Nature*, **178**, 139 (1956).
[6] Burton, W. K., Cabrera, N., and Frank, F. C., *Phil. Trans. Roy. Soc.*, **243**, 299 (1951).
[7] Frank, F. C., *Acta Cryst.*, **4**, 497 (1951).

Photochemical Stability of Dyes in the Solid State

It has recently been shown[1] that it is possible to produce level transparent dye films upon thin quartz plates by the method of vacuum deposition. This technique makes it possible to compare under similar conditions the photochemical stability of dyes in the solid state with their stability when present as a dyeing on a polymer film. For this purpose we have used several aminoanthraquinone compounds purified by repeated recrystallizations from ethyl alcohol. Polymer films were dyed with these compounds from an alcohol solution, and solid deposits upon small quartz plates were prepared with an Edwards high-vacuum coating unit. These samples were then sealed inside quartz cells through which it was possible to maintain a flow of dry oxygen or dry nitrogen (oxygen-free) continuously during exposure to a high-pressure mercury-vapour lamp (in glass) and while absorption measurements were being made on a Unicam *SP* 500 quartz spectrophotometer.

It was observed that the aminoanthraquinone compounds are much more stable to the action of near ultra-violet and visible light when present in the form of a solid film on quartz rather than as a dyeing on a polymer film. This difference in photochemical stability is illustrated in Fig. 1 by the absorption curves for 1-aminoanthraquinone on cellulose acetate film (deplasticized, British Celanese, 0·001 in. thick) and deposited on quartz, before and after exposure in dry oxygen for 2,500 hr. After irradiation the absorption of the dyed acetate film is considerably reduced at all four of the visible and ultra-violet absorption bands. Under similar exposure conditions, the changes produced in the spectrum of the solid deposit on quartz are much less. There are small reductions in the bands in the visible and near ultra-violet regions, but below 2800 A. there appears to be a slight increase in absorption. The difference in photochemical stability is even more marked with 1 : 4 diaminoanthraquinone. On cellulose acetate film there is a considerable change after irradiation in dry oxygen for 2,500 hr., with a reduction of nearly

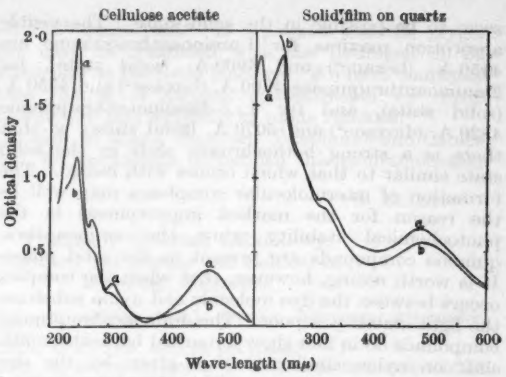

Fig. 1. 1-Aminoanthraquinone exposed to 400-W. high-pressure mercury-vapour lamp at 35° C.: *a*, unexposed; *b*, exposed 2,500 hr. in dry oxygen

one half in the intensities of the twin absorption peaks in the visible region, yet after the same exposure period there is no change at all in the spectrum of the solid film on quartz.

The effect of the presence or absence of oxygen on the photochemical stability of these compounds also seems to differ considerably between the solid state and dispersion in a polymer film. The results in Table 1 refer to the percentage decrease which occurs in the visible absorption band of 2-amino- and 1 : 5-diamino-anthraquinone after irradiation in dry oxygen or dry nitrogen. The exposure period for the cellulose acetate dyeings was only 300 hr., as compared with 2,000 hr. for the solid film on quartz, yet in both atmospheres the fading of the aminoanthraquinone compound is substantially greater with the polymer film. On the latter substrate aminoanthraquinone compounds seem to fade quite considerably in dry nitrogen; particularly is this so with 2-aminoanthraquinone. The photochemical stability in dry nitrogen seems, however, to be much greater when the dye is in the solid state. The absorption maxima for 2-amino- and 1 : 5-diamino-anthraquinone on cellulose acetate film are at 4330 A. and 4870 A., respectively.

Table 1

Anthraquinone	Decrease in visible absorption band (per cent)			
	Cellulose acetate (300 hr.)		Solid film (2,000 hr.)	
	Nitrogen	Oxygen	Nitrogen	Oxygen
2-Amino-	74	57	9	43
1 : 5-Diamino-	17	51	0	13

The photochemical stability of these aminoanthraquinone compounds is presumably dependent *inter alia* upon the mode of attachment of the dye molecules either to themselves (in the solid state) or to the polymer substrate. In this respect the views of Weinstein and Wyman[2] seem to be of importance. They have suggested that the strong bathochromic shift which is observed with the spectrum of indigo in the solid phase[3] can be taken as indicating a considerable extension of the resonating system with the formation of dimers or higher polymers in the solid phase, held together by intermolecular hydrogen bonds. The formation of similar complexes between molecules of aminoanthraquinone compounds would

seem to be possible in the solid state. The visible absorption maxima for 1-aminoanthraquinone are 4450 A. (hexane[4]) and 4900 A. (solid state), for 2-aminoanthraquinone 4300 A. (hexane[4]) and 4550 A. (solid state), and for 1 : 5-diaminoanthraquinone 4820 A. (dioxane[5]) and 5070 A. (solid state), so that there is a strong bathochromic shift in the solid state similar to that which occurs with indigo. The formation of intermolecular complexes may well be the reason for the marked improvement in the photochemical stability when the aminoanthraquinone compounds are present in the solid phase. It is worth noting, however, that when the complex occurs between the dye molecule and nylon substrate the light stability is poor. The aminoanthraquinone compounds do in fact show a marked bathochromatic shift on nylon similar to that given by the dye in the solid state, but presumably the unsymmetrical character of the complex formed is responsible for the poor photochemical stability.

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[1] Egerton, G. S., and Roach, A. G., *Nature*, **179**, 491 (1957).
[2] Weinstein, J., and Wyman, G. M., *J. Amer. Chem. Soc.*, **78**, 2387 (1956).
[3] Sheppard, S. E., and Newsome, P. T., *J. Amer. Chem. Soc.*, **64**, 2937 (1942).
[4] Lauer, K., and Horio, M., *J. Prakt. Chem.*, **145**, 273 (1936).
[5] Hartmann, H., and Lorenz, E., *Z. Naturforsch.*, **72**, 360 (1952).

Decrease in Fluorescence Intensity of a Solution of Fresh Cigarette Smoke Products on Exposure to Light

Attention has been directed by Schmähl and Schneider[1] and Druckrey and Schmähl[2] to the decrease in intensity of fluorescence which occurs when a benzene solution of fresh cigarette smoke products is exposed to light. This decrease in fluorescence indicates one obvious difference between the smoke, which will contain unchanged products when inhaled by the smoker, and any solution of the smoke products which has been exposed to light and which is then used for chemical or biological tests.

Schmähl and Schneider[1] found that the rate of decrease of intensity of fluorescence is dependent on the intensity of the light, and that ultra-violet light could cause decrease below the end-value which could be reached with daylight. It was concluded that more than one 'labile' component existed. The chemical nature of the 'labile' components was not known; but they were not thought to be aromatic hydrocarbons or alkaloids and were non-polar.

The present findings are that the 'labile' fluorescent components are products of heating the tobacco and paper, since no decrease occurs in a benzene extract of unsmoked tobacco. On heating tobacco to temperatures of 200–300° C., distillates are obtained (boiling points below 200° C.). The fluorescence intensity of a benzene solution of these distillates decreases at a similar rate to that of tobacco smoke products when exposed to light.

This phenomenon is in fact not unique to tobacco, but appears to be common to many vegetable products heated to these temperatures. 'Cigarettes' were manufactured containing sawdust, cotton-wool, cellulose powder and the dried leaves of three common weeds. When these were smoked mechanically in the same way as ordinary cigarettes the fluorescence intensity of solutions of the smoke products in benzene decreased on exposure to light. Similarly, decrease occurred with cigarettes the tobacco in which had been exhaustively extracted with concentrated acid and alkali and organic solvents. The rates of decrease were similar to that of tobacco smoke products, but the percentage of the total fluorescent material which was labile varied for the various substances. However, tobacco is the only vegetable product commonly smoked and inhaled into the lungs in this manner, and therefore this decrease in fluorescence might still be significant.

Greene[3] stated that the formation of free radicals might be expected when organic material is subjected to treatment similar to that of tobacco in cigarette smoking. Photochemical reaction such as described above suggests also a free-radical mechanism or intermediate. It is possible that some of the tars or resins in cigarette smoke products might be products of free-radical initiated polymerization; however, anhydrous aluminium chloride, which is a catalyst for ionic polymerization, proved a much more effective catalyst for the precipitation of resins from solutions of cigarette smoke products than the free-radical polymerization catalysts which were tested. Many authors have discussed the carcinogenicity of free radicals and of substances which can readily form radicals *in vivo*. It has been suggested that radicals might be detected in cigarette smoke products (Lyons, M. J., unpublished results). It is possible that the paramagnetic resonance methods of Commoner *et al.*[4] for detection of free radicals, in biological matter and in coal tar, in the presence of much diamagnetic material, might be applicable to cigarette smoke products.

I am indebted to Dr. P. R. Peacock for helpful suggestions and to the Medical Research Council for a grant.

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[1] Schmähl, D., and Schneider, H., *Arzneimittel-Forsch.*, **5**, 348 (1955).
[2] Druckrey, H., and Schmähl, D., *Science*, **122**, 421 (1955).
[3] Greene, C. R., *Science*, **123**, 227 (1956).
[4] Commoner, B., Townsend, J., and Pake, G. E., *Nature*, **174**, 689 (1954).

Oxygen as a Donor Element in Germanium

There have been a number of studies of the germanium–oxygen system from the point of view of compound formation, thermodynamics and crystal structure. Some workers have studied the effects of oxide films on the surface properties of germanium, with particular reference to conduction and rectification. However, little seems to have been published on the behaviour of oxygen as a significant doping impurity in bulk germanium. Clarke[1] observed, during experiments on the effect of oxygen on surface conduction, that after repeated exposure to oxygen, followed by heating in a high vacuum, a high resistivity germanium sample acquired a permanent larger

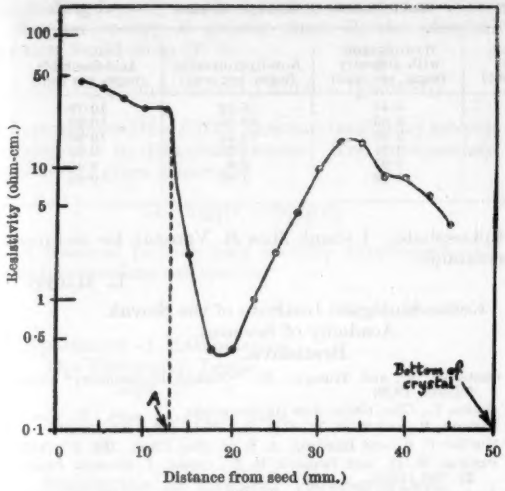

Fig. 1

n-type conductivity. This appeared to be due to the diffusion of n-type centres deep into the sample, and he suggested that oxygen might be responsible for these donor centres in the bulk while at the same time producing electron traps at the surface.

Evidence is now available that oxygen is an active donor element in germanium. This was first observed as a result of an air leak into a zone-refiner tube in which germanium was being processed in nitrogen. An intrinsic bar was converted to a very low n-type resistivity, below 0·05 ohm-cm. However, when this material was used for growing a single crystal in a hydrogen atmosphere, with a controlled amount of antimony added, the calculated resistivity, of 7 ohm-cm. near the top of the crystal, was obtained. The large amount of n-type doping agent in the original germanium had therefore been eliminated by crystal pulling in hydrogen. It was found that single crystals grown in both pure nitrogen and pure argon showed sudden changes of resistivity when small quantities of air were added to the atmosphere. The resistivity profile of a typical crystal is shown in Fig. 1. Air was admitted at point A along the length of the crystal, and the resistivity fell almost immediately from 25 to 2·1 ohm-cm., and shortly afterwards to 0·38 ohm-cm. n-type. The partial pressure of oxygen was about 15 mm. mercury. The rise in resistivity following the initial sharp drop suggests either the loss of doping agent from the melt by evaporation or a value of the distribution constant for oxygen greater than unity (compare the behaviour of boron, for example). Nitrogen is known to be inactive towards germanium in its normal molecular form[2] and is used as an inert atmosphere for processing. The activation energy of the oxygen donor level or levels remains to be determined. Armstrong, Tyler and Woodbury[3] have recently shown that selenium and tellurium, also in Group VI A, may act as double donors in germanium, and Kaiser and Keck[4] have explained donor action in silicon, associated with heat-treatment effects, as being due to the presence of oxygen. Thurmond, Guldner and Beach[5] have shown that germanium normally contains oxygen in concentrations of the order $1–3 \times 10^{18}$ atoms/cm.[3], together with hydrogen in concentrations of the order $3–8 \times 10^{16}$ atoms/cm.[3] It is possible that the oxygen here may be combined with the hydrogen in the lattice and so rendered inactive. We have confirmed these figures of oxygen concentration by direct chlorination and weighing of oxide residues.

I wish to thank Standard Telephones and Cables, Ltd., for permission to publish this communication.

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[1] Clarke, E. N., *Phys. Rev.*, **95**, 284 (1954).
[2] Billig, E., quoted by Dunlap in "Progress in Semiconductors", **2**, 182 (Heywood and Co., 1957).
[3] Armstrong, J. A., Tyler, W. W., and Woodbury, H. H., *Bull. Amer. Phys. Soc.*, Ser. 2, **2**, 265 (1957).
[4] Kaiser, W., *Phys. Rev.*, **105**, 1751 (1957). Kaiser, W., and Keck, P. H., *J. App. Phys.*, **28**, 882 (1957).
[5] Thurmond, C. D., Guldner, W. G., and Beach, A. L., *J. Electrochem. Soc.*, **103**, 608 (1956).

Changes of Organic Phosphate Esters during Glycolysis in Blood followed by a Paper Chromatography Method

The blood glucose concentration decreases very rapidly during incubation of a sample of blood *in vitro* at 37° C.[1–3]. During this glycolytic process very substantial changes take place in the content of the organic phosphate esters. These changes are related to the decrease of blood glucose, as was suggested by Paysant and Wolf[3]. Many workers have studied the behaviour of the acid-soluble phosphorus fractions in blood during incubation *in vitro*, and they have observed an increase of inorganic phosphate, a decrease of easily hydrolysable phosphate esters (this fraction represents the phosphorus largely derived from adenosine triphosphate), a decrease of phosphate fraction hydrolysable with difficulty (phosphorus released largely from hexose phosphates) and a decrease of non-hydrolysable phosphate esters (this fraction consists mainly of the 2,3-diphosphoglycerate)[3–5].

In the present communication the changes of the organic phosphate compounds of human blood during glycolysis were followed by using the paper chromatography method. Further, the behaviour of the acid-insoluble phosphorus fraction of blood (which consists of phospholipids, phosphoproteins and of phosphorus of the ribonucleic acids) was also studied.

Ten heparinized venous blood samples from healthy subjects were aerobically incubated *in vitro* at 37° C. for 24 hr. The specimens for determination of glucose concentration and of the phosphorus fractions were drawn before incubation and at the 3rd, 6th, 9th, 12th and 24th hr. during incubation. For ascendant paper chromatography of acid-soluble phosphorus compounds 0·5 ml. of blood was deproteinized with 0·5 ml. cold 10 per cent trichloracetic acid. The filtrate was neutralized by the addition of one drop of ammonium hydroxide and 0·03–0·08 ml. was applied on Watman No. 1 filter paper washed with 1 N hydrochloric acid. The solutions of known organic phosphate esters were also applied simultaneously on paper. The chromatograms were run for 14–16 hr. at 4° C. using methanol : ammonium : water as a solvent mixture[6]. After development, the chromatograms were dried at room temperature and

Table 1. The Changes of the Phosphate Fractions of Blood during Glycolysis *in vitro*

Time (hr.)	Glucose (mgm. per cent)	Inorganic phosphate (mgm. per cent)	Hydrolysable with ease (mgm. per cent)	Hydrolysable with difficulty (mgm. per cent)	Non-hydrolysable (mgm. per cent)	Acid-insoluble (mgm. per cent)
0	119	2·69	5·15	3·44	15·32	10·70
3	78	2·59	5 12	2 85	15·25	10·20
6	31	4·45	3·65	3·35	14 22	10·20
9	20	9·30	3·41	2·61	11·23	9·20
12	16	21·30	0·20	0·97	6·6	9·40
24	12	26·50	0·10	1·13	1·85	9·20

sprayed with Hanes–Isherwood acid molybdate solution[7]. After hydrolysis the chromatograms were treated with a solution of tin chloride[8].

It was found, as observed by Rohdewald and Weber[9], that the acid-soluble phosphorus fraction of human blood contains adenosine triphosphate, fructose-1,6-diphosphate, triosephosphate (mainly 2,3-diphosphoglyceric acid) in addition to inorganic phosphate (Fig. 1). During glycolysis in blood a decrease amounting to total disappearance of adenosine triphosphate, fructose-diphosphate, triosophosphate and a large increase of inorganic phosphate were observed (Table 1, Fig. 1). The inorganic phosphate was released by the progressive hydrolysis of the organic phosphate esters when the blood-glucose concentration fell below 20 mgm. per cent. No significant or substantial changes were found in the acid-insoluble phosphate fraction of blood, which points to the fact that the acid-insoluble organic phosphate compounds probably do not participate directly in the metabolic pathways of phosphorus during glycolysis in blood.

Acknowledgments are made to Messrs. Sigma Chemical Company, St. Louis, for supplying the samples of adenosine triphosphate and adenosine diphosphate. I thank Miss M. Vanščák for technical assistance.

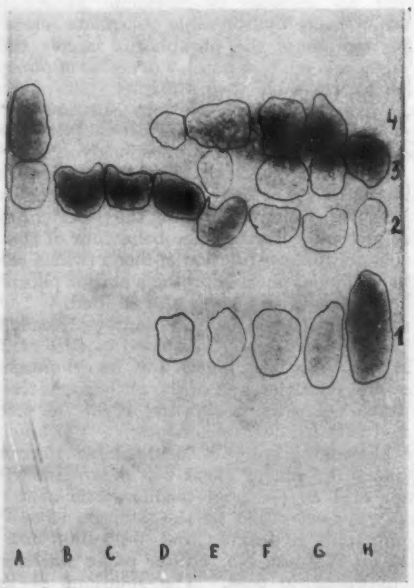

Fig. 1. The paper chromatogram of acid-soluble phosphorus compounds of blood during glycolysis in blood. The spots of known organic phosphate esters (*A*, *H* columns): (1) adenosine triphosphate, (2) inorganic phosphate, (3) fructose-1,6-diphosphate, (4) triosephosphate. The samples of blood before the incubation (*G*), after 3 hr. (*F*), 6 hr. (*E*), 9 hr. (*D*), 12 hr. (*C*) and after 24 hr. (*B*) of incubation of blood at 37° C.

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[1] Cantarow, A., and Trumper, M., "Clinical Biochemistry" (Philadelphia, 1949).
[2] Macho, L., *Clin. Chim. Acta* (in the press).
[3] Paysant, P., and Wolf, R., *C.R. Soc. Biol.*, **146**, 1250 (1952).
[4] Mueller, C. B., and Hastings, A. B., *J. Biol. Chem.*, **189**, 881 (1951).
[5] Pappius, M. H., and Densted, O. F., *Canad. J. Biochem. Physiol.*, **32**, 293 (1954).
[6] Axelrod, B., and Bandurski, R. S., *J. Biol. Chem.*, **195**, 405 (1951).
[7] Hanes, C. S., and Isherwood, F. A., *Nature*, **164**, 1107 (1949).
[8] Macho, L., *Chemické Zvesti*, **11**, 175 (1957).
[9] Rohdewald, M., and Weber, M., *Hoppe-Seyler's Z. Physiol. Chemie*, **306**, 95 (1957).

Classical Motion under a Morse Potential

Students of diatomic molecules and of related systems have long used the Morse potential function[1]

$$V(x) = D\{1-\exp(-ax)\}^2 \qquad (1)$$

where x is the stretch of the interatomic bond (with $V=0$ at the equilibrium configuration $x=0$), D is the dissociation energy, and a a constant parameter. For energies less than D and no rotation, Morse gave the quantum energy levels of (1), namely

$$E_n = (n+\tfrac{1}{2})h\nu_0 - \{(n+\tfrac{1}{2})h\nu_0\}^2/4D, \quad n=0,\ 1,\ 2,\ldots \qquad (2)$$

where $\nu_0 \equiv (a/2\pi)(2D/\mu)^{\frac{1}{2}}$ is the frequency of classical small vibrations, μ being the reduced mass of the two bonded atoms.

Just as the quantum levels (2) are closely related to those of the harmonic oscillator, so also there is a close relation between the classical Newtonian motion under (1) and that of the harmonic oscillator. I found that Prof. Morse was aware of this; but he suggested that it should be made more widely known. The classical energy equation for the relative rectilinear motion of the two atoms is

$$\tfrac{1}{2}\mu(dx/dt)^2 + D\{1-\exp(-ax)\}^2 = E \qquad (3)$$

If the energy E is less than D, then integration (for example, using $\exp(ax)$ as variable) gives

$$ax = \log[\{1-\cos\theta\cos(2\pi\nu_0 t\sin\theta)\}/\sin^2\theta] \qquad (4)$$

where $\cos^2\theta = E/D$, and the time t is measured from the position of minimum x. Thus the classical motion is periodic, and may be described as the logarithm of simple harmonic motion. The frequency of vibration at energy E is, from (4),

$$\nu = \nu_0\sin\theta = \nu_0\{(D-E)/D\}^{\frac{1}{2}}$$

tending to zero as E approaches D. If E has a value E_n as in (2), the classical motion has frequency

$$\nu = \nu_0\{1-(n+\tfrac{1}{2})h\nu_0/2D\}$$

depending linearly on the quantum number n.

For an energy E greater than D, the classical motion found from (3) is

$$ax = \log[\{\cosh\theta\cosh(2\pi\nu_0 t\sinh\theta) - 1\}/\sinh^2\theta)]$$

where now $\cosh^2\theta = E/D$. This non-oscillatory motion corresponds to dissociated states. The intermediate case $E = D$ gives classically

$$ax = \log\tfrac{1}{2}\{1 + (2\pi\nu_0 t)^2\}$$

This classical picture may usefully supplement the quantum-mechanical results.

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[1] Morse, P. M., *Phys. Rev.*, **34**, 57 (1929).

Prediction of Critical Temperatures

In cases where critical temperatures are unknown they can be calculated from a number of empirical or semi-empirical formulæ[1], the simplest but least-accurate being Guldberg's rule. More accurate equations exist for estimating values for hydrocarbons, for example, those of Jatkar and Lakshminarayanan[2] and Watson[3], but these are unsuitable for use with phenolic and basic organic compounds which occur in coal tar.

The critical temperatures of fourteen paraffins, twenty-five aromatic hydrocarbons, four phenols and seven organic bases[4–6] have been correlated in these laboratories with the boiling point and density of the respective compounds[7,8] by the method of least squares. As a result it was found that the following equation predicts values in the range 260–530° C. with an accuracy of ±20·8° C., that is, with an average of ±5 per cent, with 95 per cent confidence:

$$t_c = 221{\cdot}6 + 1{\cdot}029\ t_b\ d_{20}$$

where t_c is the critical temperature (°C.), t_b is the boiling point (°C.), and d_{20} is the density at 20° C. (gm./ml.). (In the case of solids, liquid values were extrapolated back to 20° C.)

The major discrepancies are given by five hydrocarbons the omission of which reduces the limits of error to ±14·2° C.

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[1] Partington, J. R., "An Advanced Treatise on Physical Chemistry", 646 *et seq.* (Longmans, Green and Co., London, 1949).
[2] Jatkar, S. K. K., and Lakshminarayanan, D., *J. India Inst. Sci.*, **28**, A, 1 (1946).
[3] Watson, K. M., *Indust. Eng. Chem.*, **23**, 360 (1931).
[4] "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds", A.P.I. Research Project 44 (1953).
[5] Doss, M. P., "Physical Constants of the Principal Hydrocarbons" (The Texas Co., New York, 1943).
[6] Ambrose, D., and Grant, D. G., *Trans. Farad. Soc.*, **53**, 771 (1957).
[7] Coal Tar Research Association, "The Coal Tar Data Book" (Gomersal, C.T.R.A.).
[8] Egloff, G., "Physical Constants of Hydrocarbons" (Reinhold Pub. Corp., New York, 1946).

X-Ray Microscopy of Human Dental Pulp Vessels

Microradiographic studies of the human dental pulp vessels were prompted by the inadequate anatomical information on the pulpal vascular patterns, and by the statement that these vessels could not be visualized radiographically[1]. However, it has been shown that fine-contrast media of particle size 0·1–0·5μ (for example, 'Thorotrast', 'Micropaque') can be introduced by suction injection into the human dental pulp vessels and their vascular patterns demonstrated microradiographically[2].

Good results have been obtained by contact microradiography using a standard Philips 'Norelco' X-ray diffraction tube and an Ehrenberg–Hilger microfocus tube, with an effective focal spot of 1 mm. and 0·04 mm. respectively. The contact method, however, is limited partly by the size of the X-ray source and the grain-size of the recording emulsion, while the resolution cannot exceed that of the optical system used for enlarging the X-ray negative.

Recently better resolution and contrast, with consequently sharper image definition of all the vessels in the dental pulp, have been obtained by the projection method, using the X-ray projection microscope developed by Cosslett and Nixon[3]. The marked primary magnification (up to × 200 or higher) obtainable with this instrument, coupled with the high resolution afforded by its point source of X-ray emission (less than 1μ), makes it possible to image the smallest capillaries within the human tooth with great clarity.

This X-ray microscope has distinct advantages over the optical microscope in such dental studies by virtue of its penetration and depth of field. Its great focal depth results in all parts of the specimen being in focus, and permits the taking of stereomicrographs by shifting the specimen laterally between two exposures.

A section of human dental (bicuspid) pulp imaged in juxtaposition to a piece of 1,500 mesh silver grid,

Fig. 1. X-ray micrograph of human dental pulp showing the capillaries of the subdentinal plexus imaged with 1,500 mesh silver grid

composed of 3μ bars with 17μ mesh spaces, illustrates the calibre of vessel demonstrable by X-ray microscopy (Fig. 1), showing as it does the smallest capillaries of the subdentinal plexus.

Other medical studies[4] have already made it clear that X-ray microscopy is capable of providing a detailed and dynamic picture of the minutest vessels that constitute the peripheral vascular system. New angiographic techniques used in conjunction with the X-ray projection microscope are now making it possible to observe vascular changes in living tissue (rabbit ear) under experimental treatment. This instrument produces microangiograms of even greater clarity than hitherto, and allows the demonstration of reactions in even the smallest vessels.

This work has been conducted under grants from the National Research Council of Canada. I wish to thank Dr. W. C. Nixon for many useful discussions, and also Miss R. M. Frye and Mr. C. K. Jackson for their help.

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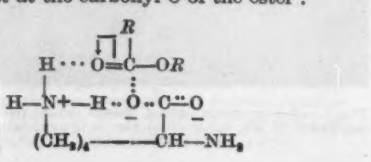
[1] Boling, L. R., *Anat. Rec.*, **82**, 25 (1942). Kramer, I. R. H., *ibid.*, **111**, 91 (1951).
[2] Saunders, R. L. de C. H., Proceedings of the Cambridge Symposium on X-Ray Microscopy and Microradiography, 1956 (Academic Press, New York).
[3] Cosslett, V. E., and Nixon, W. C., *Nature*, **168**, 24 (1951); *Proc. Roy. Soc.*, B, **140**, 422 (1952); *J. App. Phys.*, **24**, 616 (1953).
[4] Saunders, R. L. de C. H., Proceedings of the Cambridge Symposium on X-ray Microscopy and Microradiography, 1956 (Academic Press, New York). Redisch, W., Tangco, F. F., and Saunders, R. L. de C. H., "The Peripheral Circulation in Health and Disease" (Grune and Stratton, New York, 1957).

Chemical Model of a Biological Reaction

We were searching for a model of an enzymatic reaction in the hope that the relatively simple chemistry of the model reaction might throw some light on the enzyme reaction itself. In particular, we were interested in finding a model which would duplicate some of the properties of lipases, notably their ability to catalyse the hydrolysis of lipids and the characteristic *p*H dependence of lipolytic activity which reaches a maximum near *p*H 8·5 with most lipases, and one just below *p*H 7 with some. Lipases being proteins, the model would have to be restricted to the functional groups available in proteins. The high potency of lipases, despite this restriction, together with the well-known chemical mechanism of ester hydrolysis, made us suspect that bifunctional catalysis[1] might play a decisive part.

Examination of high-precision atom models[2] disclosed the fact that the ε-ammonium group of lysine is sterically capable of forming a hydrogen bond with the carboxylate group of the same molecule, and that such a —COO^-. . .H_3N^+— bonded structure exactly fits an ester group in a fashion suitable for bifunctional catalysis, so that a proton of the ammonium group functions as an acidic catalyst at the carbonyl O of the ester and the carboxylate O of the lysine as a basic catalyst at the carbonyl C of the ester:



It stands to reason that the hydrogen bonds which the ε-ammonium group is to form with the carboxyl group of lysine and the O of the ester should be strongest when the N does not hold its hydrogens too tightly, because that is when they will be most readily donated for a hydrogen bond. Such would be the case just below the *p*H at which the ε-ammonium group of lysine loses a hydrogen and its positive charge. That happens at *p*H 9·5, so that lysine should be maximally active as a catalyst for ester hydrolysis around *p*H 8–9.

Similar reasoning could hold also for histidine, which, however, has no $-NH_3^+$, only two —NH— groups with one positive charge spread over them. If the H of either —NH— group is used up to form a (sterically possible) hydrogen bond with the histidine carboxyl, this H is no longer available for hydrogen bonding to the substrate, and the other —NH— is too far away to act in concert with the $-COO^-$. If histidine is to be lipolytic, its carboxyl group is more likely to be attracted to the positively charged ring as a whole, which leaves the —NH— groups free to form hydrogen bonds elsewhere. This arrangement is sterically able to catalyse ester hydrolysis but with less hydrogen bonding and poorer fit than lysine. Histidine should therefore be a weaker lipolytic agent, with an optimum somewhat below the isoionic point of histidine, that is, around *p*H 6–7.

The foregoing speculation was tested by measuring the rate of hydrolysis of tributyrin according to Alper's method[3] for the assay of lipases, but using lysine or histidine in 1 per cent concentration instead of lipase. As graphically shown in Fig. 1, the results bear out our expectations, inasmuch as both lysine and histidine are capable of catalysing the hydrolysis of the test lipid, tributyrin, lysine being far more potent, and both amino-acids having maximum activity exactly at the expected *p*H.

We also tested glycine in the same experimental arrangement and found no lipolytic activity. Thus it appears that such activity is specific to lysine and histidine (and possibly to some other amino-acids) but cannot be a general property of all amino-acids.

We were impressed by the fact that the *p*H optima which we postulated for the lipolytic activity of lysine

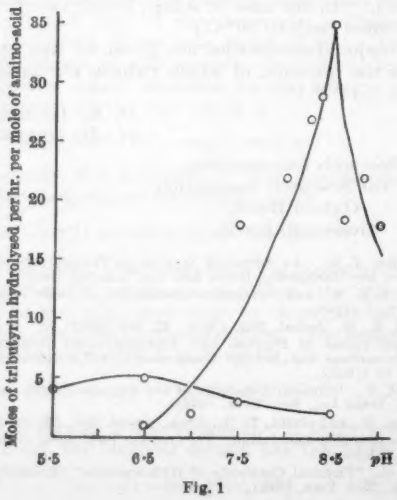


Fig. 1

and histidine, and which were confirmed by the experiment, are also the *p*H optima of the natural lipases. The question arises whether the lipolytic activity of lysine and histidine has any relevance to that of the lipases, that is, whether lysine and histidine are also lipolytic when within a polypeptide chain. (Note that the postulated lipolytic mechanism of both these amino-acids involves only one O of the carboxyl group and not at all the α-amino group.) The attractiveness of this idea lies in the circumstance that it accounts for lipolytic activity in a protein without calling on any other factors than two amino-acids ubiquitous in proteins, and that it explains the *p*H optima of the lipases. Against the hypothesis must be held the fact that not all proteins are lipases, but those that are, are much more potent catalysts of lipid hydrolysis than are lysine and histidine. However, both these amino-acids are highly hydrophilic and therefore at a disadvantage in attacking lipids. If they are to be important in the activity of those polypeptides which act as lipases, the rest of the polypeptide molecule must be equally important in providing the means—for example, van der Waals bonds—by which the catalyst attaches itself to the substrate and allows the active portion of the polypeptide to attack the ester group of the lipid.

Likewise, specific esterases could operate by means of a lysine or histidine radical attached to such other amino-acids as are optimal for attachment to the specific substrate in question.

Experiments designed to explore these possibilities are now in progress, and their results will be reported from time to time.

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[1] Swain, C. G., *et al.*, *J. Amer. Chem. Soc.*, **70**, 1119 (1948); **74**, 2534, 2538 (1952).
[2] Gero, A., *J. Org. Chem.*, **16**, 1222 (1951); *Science*, **119**, 112 (1954).
[3] Alper, C., in Reiner, M., "Standard Methods of Clinical Chemistry", **1**, 71 (Academic Press, New York, 1953).

Anion Exchange Chromatography and Molecular Size of Deoxyribonucleic Acid

IN conjunction with investigations on deoxyribonucleic acid isolated from white blood cells of patients with leukæmia (Polli, E. E., Rosoff, M., di Mayorca, G., and Cavalieri, L. F. (unpublished) and ref. 1), an interesting correlation was found between the molecular parameters of the acid and their chromatographic profiles obtained by fractionation on columns of 'Ecteola'[2].

Specimens of deoxyribonucleic acid were prepared from the white blood cells of two patients with chronic lymphatic leukæmia who had been treated with X-rays. The acid from each patient was prepared both by a detergent method[3] and the Sevag amyl alcohol–chloroform procedure[4]. Analyses by the Sakaguchi method for possible residual protein contamination indicate less than 0·05 per cent protein in both types of preparations. Chromatography on columns of 'Ecteola' of the samples of deoxyribonucleic acid obtained from one patient gave the different patterns shown in Fig. 1. (Patterns nearly identical to these were obtained with the samples of deoxyribonucleic acid from the second patient.) The differences in the chromatographic profiles are especially evident in regions I and III.

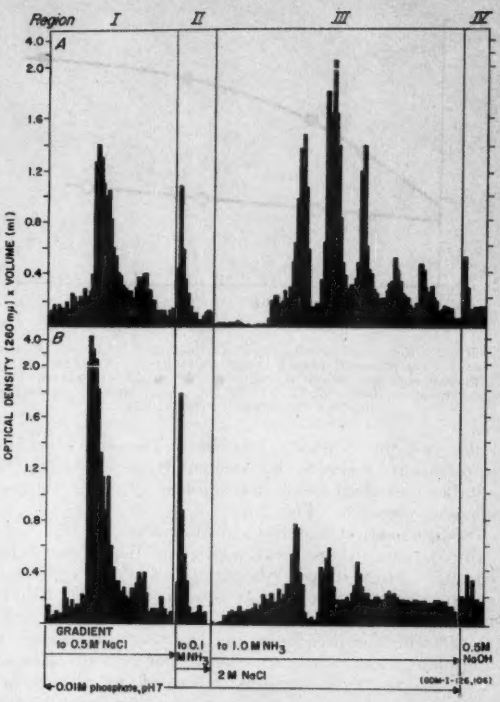

Fig. 1. Anion exchange chromatographic fractionation of 3·0 mgm. of deoxyribonucleic acid from white cells of patients with chronic lymphatic leukæmia (X-ray treated) on 0·5 gm. columns (0·8 × 5·9 cm.) of 'Ecteola' (Ecteola-SF-1, 0·51 per cent N, 0·20 meq. ionizing groups/gm., flow-rate about 6 ml./hr., 2-hr. collections). The black areas shown are directly proportional to the weight of deoxyribonucleic acid. Upper profile (*A*) is for deoxyribonucleic acid isolated by a detergent procedure (ref. 3); recovery 93 per cent. Lower profile (*B*) is for that isolated by the amyl alcohol–chloroform procedure (ref. 4); recovery 94 per cent

With the detergent procedure (Fig. 1*A*), regions I and III contained, respectively, 30 and 62 per cent of the added deoxyribonucleic acid. In contrast, regions I and III from the Sevag-treated sample contained, respectively, 67 and 18 per cent (Fig. 1*B*).

Light-scattering and viscosity data are given in Table 1.

Table 1. DEOXYRIBONUCLEIC ACID FROM THE WHITE BLOOD CELLS OF A PATIENT WITH CHRONIC LYMPHATIC LEUKÆMIA

Isolation procedure	Amyl alcohol–chloroform method (ref. 4)	Detergent method (ref. 3)
Molecular weight	$3·0 \times 10^6$	$4·0 \times 10^6$
Radius of gyration	1800 A.	2200 A.
Intrinsic viscosity, 100 ml./gm.	30	37
Sedimentation coefficient	16	25

Light-scattering was measured in a Brice–Phoenix photometer; viscosities were determined in a Couette viscometer based on Eisenberg's design[5]; weight-average sedimentation coefficients were determined in a 'Spinco' Model *E* ultracentrifuge[6].

The lower molecular weight for the alcohol–chloroform preparation is in accord with the results of Shooter and Butler[6], who showed by sedimentation analysis with deoxyribonucleic acid of calf thymus that the Sevag procedure leads to the removal of material containing the acid of high sedimentation coefficient. Additional evidence that a higher mole-

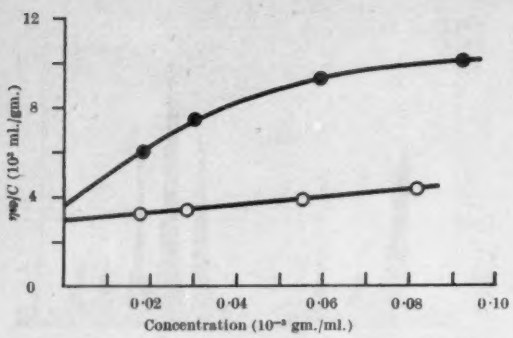

Fig. 2. Reduced viscosity of deoxyribonucleic acid from white cells of a patient with chronic lymphatic leukæmia (X-ray treated). Plotted against concentration. ●—●—●, Acid isolated by detergent method (ref. 3); ○—○—○, acid isolated by amyl alcohol–chloroform method (ref. 4)

cular weight fraction has been removed by the application of the Sevag method is provided by the smaller concentration dependence of the reduced specific viscosity (Fig. 2).

Sedimentation distribution analyses of the present samples are in essential agreement with the prior results obtained by Shooter and Polli (personal communication) on similar specimens. The results indicate that about 35 per cent of material with $S>26$ which is present in the Dounce[3] preparation is completely lost, while another 20 per cent of material with $S=21$–26 is partially removed by the Sevag treatment. It is suggestive to compare the 55 per cent loss, calculated from the sedimentation distribution, with the parallel loss of 44 per cent of the material from region III of the chromatogram of the Dounce preparation. It thus appears that region III represents material with sedimentation coefficients between 21 and 54, and region I those fractions with S between 8 and 21.

Since the distribution in sedimentation coefficients reflects a distribution in shape as well as molecular size, it is likely that fractions with $S>26$ may not possess molecular weights as high as those which can be calculated if the relationship $S \propto M^{1/3}$ is assumed[7]. The small difference in the intrinsic viscosities of both samples as well as in the radii of gyration indicates that the higher sedimenting components have a more compact configuration. (The radius of gyration determined by light scattering is a z-average quantity and therefore very sensitive to the presence of small amounts of material of highly extended configuration.) Indeed, a difference of one million in the molecular weight of the two samples would correspond only to the loss of fractions with a weight average molecular weight of about five million.

It is concluded from these studies that the loss of material with higher molecular weight and relatively greater extensibility has resulted in the alterations in the chromatographic profile. This offers further support for the contention[8] that molecular size and shape are important factors in the fractionation of deoxyribonucleic acid by 'Ecteola'-chromatography.

We wish to thank Dr. G. B. Brown and Dr. E. E. Polli for helpful discussions and Mr. H. S. Rosenkranz for competent assistance. One of us (G. D. M.) holds a Damon Runyon Cancer Research Fellowship. This investigation was supported by funds from the American Cancer Society, National Cancer Institute, National Institutes of Health, Public Health Service (Grant *CY*–3190), and from the Atomic Energy Commission (Contract No. *AT*. (30–1), 910).

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[1] Polli, E. E., and Semenza, S., *Biochem. Z.*, **327**, 231 (1955).
[2] Bendich, A., Fresco, J. R., Rosenkranz, H. S., and Beiser, S. M., *J. Amer. Chem. Soc.*, **77**, 3671 (1955). Bendich, A., Pahl, H. B., and Beiser, S. M., *Cold Spring Harbor Symp. Quant. Biol.*, **21**, 31. (1956).
[3] Kay, E. R. M., Simmons, N. W., and Dounce, A. L., *J. Amer. Chem. Soc.*, **74**, 1724 (1952).
[4] Chargaff, E., Lipshitz, R., Green, C., and Hodes, M. E., *J. Biol. Chem.*, **192**, 223 (1951).
[5] Eisenberg, A., and Frei, E. H., *J. Polymer Sci.*, **14**, 417 (1954).
[6] Shooter, K. V., and Butler, J. A. V., *J. Polymer Sci.*, **23**, 705 (1957); *Trans. Farad. Soc.*, **52**, 734 (1956).
[7] Oth, A., Conférences et Rapports P. 142, 3ème Congrès International de Biochimie, Bruxelles (1955).
[8] Bendich, A., Pahl, H. B., Rosenkranz, H. S., and Rosoff, M., Soc. Exp. Biol. Symp., **12**, Sept. 16–20, 1957 (in the press).

A Phenol-extracted Bacterial Deoxyribonucleic Acid

In the course of extraction of highly polymerized bacterial deoxyribonucleic acid from *Brucella abortus* cells first killed with 0·5 per cent phenol and then exposed to sodium deoxycholate, it was discovered that phenol treatment alone results in the recovery of material high in content of deoxyribonucleic acid. The acid isolated by this phenol procedure proved to possess specific transforming activity. Its breakdown products exerted selective effects upon bacterial population changes[1,2]; they also reduced the *LD*50 of pneumococci for mice[3] and enhanced phagocytosis *in vitro* (Pomales-Lebrón, A., Braun, W., and Stinebring, W., unpublished results); they also stimulated the growth of lymphosarcoma cells in mice. The polymerized material produced antibodies that appear to show a specificity for the deoxyribonucleic acid molecule[3]. In view of these diverse biological effects, additional details regarding the phenol extraction procedure and some characteristics of the resulting material will be presented here.

Bacterial cells are harvested from growth on tryptose agar in ten Blake bottles (100 ml. medium per bottle). The growth from each bottle is washed off with 10 ml. of a 0·1 *M* sodium citrate – 0·1 *M* sodium chloride solution. The pooled cell suspensions (approximately 1×10^{11}/ml.) are then supplemented with melted crystalline phenol to yield a phenol concentration of 0·5 per cent. The phenolized suspensions (100 ml.) are shaken, gently enough to avoid foaming, for 48 hr. at 37° C. in a 1,000-ml. Erlenmeyer flask with 100 ml. of 4-mm. glass beads. (Various stages of the extraction procedure at which samples were removed for analysis will be designated *A*–*E*.) The suspensions (*A*) then are treated with 0·1 vol. amyl alcohol (10 ml.) and 0·3 vol. (30 ml.) of chloroform[4]. The mixture is shaken for 20 min., distributed into centrifuge tubes, and centrifuged at 1,500 r.p.m. at 5° C. for 20 min. The supernatant is decanted and set aside in the refrigerator. The sediment is then re-extracted by adding to the total sediment from the first extraction 100 ml. of citrate–saline and then amyl alcohol and chloroform as above; this is shaken for 20 min. and centrifuged at 5° C., and the resulting supernatant is pooled with the supernatant from the first extraction (*B*). To the pooled super-

natants is added 0·3 vol. of chloroform (60 ml.) and 0·1 vol. (20 ml.) of amyl alcohol. Again, the mixture is shaken for 20 min., the layers are permitted to separate, the top layer is decanted and then recentrifuged in the cold (*C*) (chilling prior to centrifugation will ease decanting). This procedure may be repeated (*D*) as often as four to five times until, on the basis of non-cloudiness in the supernatant and absence of an intermediate ('protein') layer, deproteinization appears to be complete. However, more recent studies have indicated that such continued deproteinization is unnecessary for biological effectiveness. To the supernatant from the final 'deproteinization', 6 vol. of 95 per cent ethyl alcohol are added. The resulting fibrous precipitate is removed by winding on a glass rod, and is dissolved in approximately 150–200 ml. of saline (*E*); overnight storage at 5° C. plus shaking may be necessary to dissolve the material. The deoxyribonucleic acid–saline solution is assayed[5] and divided into aliquots equalling approximately 10 mgm. of the acid (mucoid cells of *Br. abortus*, strain 19, harvested from 10 Blake bottles yield an average of 60 mgm. deoxyribonucleic acid). The acid from each of these aliquots is then reprecipitated by addition of 6 vol. of 95 per cent ethyl alcohol; the precipitates are removed by winding on a glass rod and placed separately into vials containing 10 ml. of 95 per cent ethyl alcohol for storage at 5° C. For use, the material is removed by decanting the alcohol and dissolved in saline.

The deoxyribonucleic acid nature of the resulting material has been indicated by ultra-violet absorption, viscosity measurements, susceptibility to deoxyribonuclease action, positive Dische–Stumpf reaction and chromatography for pyrines and pyrimidines following hydrolysis. Absorption in the ultra-violet range showed a maximum at 258 mμ and minima at 234 and 290 mμ in 0·85 per cent saline, similar minima and a maximum at 260 mμ with an ε (*P*) of 8,900 in 0·15 *M* acetic acid. Intrinsic viscosity in 0·2 *N* sodium chloride at 35·4° C., measured with an Ostwald viscosimeter, was 16 and decreased to 50 per cent within 200 sec. following treatment with deoxyribonuclease (Worthington 1 × crystallized). Under identical conditions calf thymus deoxyribonucleic acid prepared according to Kay *et al.*[6] had an intrinsic viscosity of 19. Ribonucleic acid was found[7] to represent less than 1·5 per cent of the final material. However, a considerable amount of protein, apparently difficult to dissociate by conventional deproteinization procedures, was found to remain associated with the deoxyribonucleic acid. Biuret tests indicated approximately 25 per cent protein at stage *B*. Similarly, a high nitrogen/phosphorus ratio at this stage of purification pointed to the retention of considerable protein (Table 1). It is noteworthy that with further treatment by the Sevag procedure the nitrogen/phosphorus ratios shifted in the direction of increased nitrogen (Table 1). Similar alterations, probably indicative of a loss of deoxyribonucleic acid during the amyl alcohol–chloroform deproteinization procedure, previously have been observed by others for calf thymus nucleic acid[8]. The unusually high nitrogen/phosphorus ratios might also reflect differences between the nitrogen–phosphorus content of this bacterial deoxyribonucleic acid and values established for calf thymus deoxyribonucleic acid. The protein present was found to contain at least 15 amino-acids, on the basis of qualitative paper chromatography following hydrolysis of stage *B* material. Nitrogen/phosphorus ratios obtained for deoxyribonucleic acid isolated from smooth cells of *Br. abortus* tended to be slightly higher than those recorded here for material from mucoid cells and showed similar changes during purification. The phenol-extracted material was completely but slowly soluble in 0·85 per cent saline and could be reprecipitated almost quantitatively from the resulting viscous solution by the addition of ethyl alcohol.

Table 1. Chemical Analyses on Two Preparations of Deoxyribonucleic Acid obtained from Mucoid *Br. abortus* Cells

		Extraction stages analysed (ref. 5)				
		A	*B*	*C*	*D*	*E*
Preparation 1	N/P	2·86	2·18	2·60	3·03	4·17
	DNA/N	2·48	2·95	2·59	2·12	2·20
	DNA/P	7·07	6·44	6·74	6·42	9·17
Preparation 2	N/P	2·94	2·29	2·39	3·33	5·00
	DNA/N	2·44	2·94	1·81	1·71	2·10
	DNA/P	7·18	6·68	4·34	5·67	10·50

The 0·5 per cent phenol extraction procedure has been applied successfully to the isolation of deoxyribonucleic acid from *Escherichia coli* cells, pneumococci, salmon sperm and mouse lymphosarcoma ascites cells. The use of the method with calf thymus required prior exposure of homogenized tissue to 6 *M* sodium chloride.

Although the resulting material most closely resembles deoxyribonucleic acid and has been referred to as such, and despite indications that all hitherto tested biologic and antigenic effects of the material appear to be independent of the amount of protein remaining, it is recognized that the procedure here described might actually lead to the isolation of an unusually stable nucleoprotein.

The co-operation of Drs. W. Nickerson and J. Noval in the viscosity determinations, of Dr. J. Noval in the protein tests, and of Mr. W. Firshein in ribonucleic acid assays, is gratefully acknowledged. Part of this study was supported by grants from the National Science Foundation (*G*-2184) and the U.S. Public Health Service (*E*-1137).

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[1] Braun, W., and Whallon, J., *Proc. U.S. Nat. Acad. Sci.*, **40**, 162 (1954).
[2] Braun, W., Firshein, W., and Whallon, J., *Science*, **125**, 445 (1957).
[3] Phillips, J. H., Braun, W., and Plescia, O. (in the press).
[4] Sevag, M., Lackman, D., and Smolens, J., *J. Biol. Chem.*, **124**, 425 (1938).
[5] Stump, P. R., *J. Biol. Chem.*, **169**, 367 (1947).
[6] Kay, E. R. M., Simmons, N. S., and Dounce, A. L., *J. Amer. Chem. Soc.*, **74**, 1724 (1952).
[7] Webb, J. M., *J. Biol. Chem.*, **221**, 635 (1956).
[8] Frick, G., *Biochim. Biophys. Acta*, **13**, 41 (1954).

Action of Glucose-1-Phosphate on the Deposition of Phosphate in the Bones of Growing Diabetic Rats

It has been shown in a previous paper[1] that the ossification process of growing diabetic rats is strongly retarded in comparison with normal animals and that the administration of insulin restores the ossification process to a normal rate. An even more pronounced effect was obtained by daily injections of 1–2 gm./kgm.

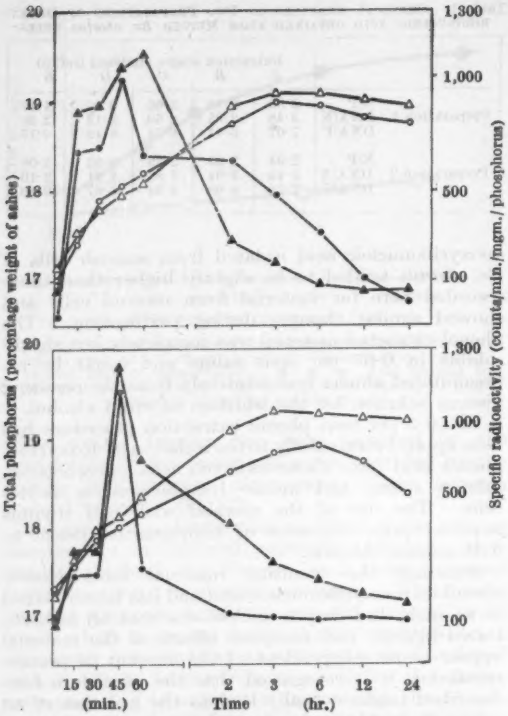

Fig. 1. Above: Normal animals; below: diabetic animals. ●, Total phosphorus after injection of 3·3 μmole/kgm. $NaH_2{}^{32}PO_4$; ▲, total phosphorus after injection of 3·3 μmole/kgm. glucose-1-^{32}phosphate; ○, specific radioactivity of phosphorus-32 after injection of 3·3 μmole/kgm. $NaH_2{}^{32}PO_4$, corresponding to a 10-μc. radioactivity; △, specific radioactivity of phosphorus-32 after injection of 3·3 μmole/kgm. glucose-1-^{32}phosphate, corresponding to a radioactivity of 10 μc. Full point represents the mean value of data obtained from five animals

of glucose-1-phosphate over a period of 10–15 days. The ready response to glucose-1-phosphate suggested that the impairment of ossification in diabetes might be attributed to a possible glucose-1-phosphate deficiency and that this ester might act as phosphate carrier or donor in phosphate deposition in the bones.

It is the object of the present communication to test this hypothesis: to this end the behaviour of the total phosphorus and of phosphorus-32 content of bones was examined at different time-intervals after the administration of glucose-1-^{32}phosphate.

Experiments were carried out on normal 2-months-old rats (approximately 80 gm. body-weight) fed on a calcium-rich diet and on rats of the same age and weight which had been made diabetic by intravenous injections of alloxan (100 mgm./kgm. body-weight). No rat was used less than two weeks after alloxan administration.

Glucose-1-phosphate-^{32}P, kindly supplied by the firm S.P.A. of Milan, was injected intraperitoneally at a dose of 1·1 gm./kgm. body-weight, corresponding to a radioactivity of 10 μc./kgm. As control, an equal number of normal and diabetic animals were injected, with equal amounts of phosphorus and of phosphorus-32 in the form of $NaH_2{}^{32}PO_4$.

At various time-intervals after the injection the rats were killed and the bones of the hind limbs quickly removed and ashed. The total phosphorus of the ash was determined by the Fiske and Subbarow procedure and the specific radioactivity using a Nuclear-Chicago Corp. counter.

The results relative to the normal and diabetic animals are respectively illustrated in Fig. 1, *A* and *B*. These results show that while in normal animals the administration of either $NaH_2{}^{32}PO_4$ or of glucose-1-phosphate-^{32}P influences the deposition of the phosphate in the bones practically at the same rate, in diabetic animals glucose-1-^{32}phosphate exhibits a more pronounced effect than $NaH_2{}^{32}PO_4$.

The possibility that the higher utilization of glucose-1-phosphate by diabetic animals might be due to a gradual release of inorganic phosphate radicals from glucose-1-phosphate should be excluded because the phenomenon is not apparent in normal animals. It seems therefore reasonable to assume that the bones of growing diabetic rats utilize the phosphorus of glucose-1-phosphate better than that of inorganic phosphates.

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[1] De Bastiani, G., and Petrelli, F., *Boll. Soc. Eustachiana dell'Universita di Camerino* (in the press).

Action of Ethylene Dibromide on Hen Gonadotrophic Hormones

Ethylene dibromide (dibromoethane) was found to remain in small amounts in fumigated grain up to six weeks after fumigation[1]. This fact, unusual for fumigants, had a harmful effect on laying hens. Diminution in size of egg, followed by cessation of laying were observed. Significant decrease in weight of egg occurred even when grain containing 15 p.p.m. of ethylene dibromide was fed to laying hens over 12 weeks[2]. The total amounts of ethylene dibromide ingested by such hens were well below those reported as harmless to various laboratory animals[3,4]. The following observations lead to the hypothesis that the action of small amounts of ethylene dibromide is very specific on pituitary gonadotrophic hormones and should be distinguished from the general poisonous action of large doses.

The general behaviour of hens fed with grain containing ethylene dibromide was normal, and no specific changes could be detected by autopsy. The ovaries of hens which stopped laying were found to contain follicles of small size similar to those of young hens before the laying season. A few eggs laid occasionally by such adult hens, several months after stopping the treatment with ethylene dibromide, weighed only 16–20 gm. The yolk of these eggs was extremely small and the relation between weights of yolk and egg white was about 1 : 4 (instead of about 1 : 2 in normal eggs). It is known that the size of eggs is conditioned mainly by the size of ovulated follicles.

From the two principal gonadotrophic hormones—the follicle-stimulating hormone and the luteinizing hormone—the former should have been primarily affected, because ethylene dibromide could be dosed so as to obtain only decrease of egg weight, without

changes in their number. Ovulation apparently proceeded normally.

Furthermore, it was assumed that formation (or release) of follicle-stimulating hormone is affected by ethylene dibromide rather than the hormone itself, after it has left the pituitary. This assumption arose from an observation that hens laying small eggs after treatment with ethylene dibromide recovered only after several weeks of normal feeding.

The following experiments were performed to prove this hypothesis.

(1) 10 hens (15 months old) were fed with grain containing ethylene dibromide until they were laying eggs smaller by 30–40 per cent from the mean before the treatment. Then the hens were divided into two groups. One group received daily, during 11 days, one injection of 14 mgm. follicle-stimulating hormone preparation in 0·5 c.c. 0·9 per cent sodium chloride (7·2 mgm. purified follicle-stimulating hormone, *S* 70*A*, prepared and kindly donated by W. McShan, were equivalent to 1 gm. dry pituitary tissue). The second group remained as control group. In the group treated with the hormone an increase of 10–15 per cent in egg-weight occurred 6–7 days after beginning of hormone injections and persisted up to 4–6 days after stopping the treatment. At this time the egg returned to former smaller size. It is known that the process of follicle growth in the ovary takes about 10 days. The eggs of the control group (hens treated only with ethylene dibromide, but not with hormone) showed no increase during the experimental period.

(2) The follicle-stimulating hormone preparation mentioned above was exposed to ethylene dibromide vapours for 24 hr. and then injected in the usual way to a group of five female albino rats[5]. Another group of rats received the untreated hormone.

After total amount of 1·4 mgm. follicle-stimulating hormone per rat the average ovary-weights were :

47 ± 2 mgm. for the group receiving untreated follicle-stimulating hormone
46 ± 1 mgm. for the group receiving follicule-stimulating hormone treated by ethylene dibromide
28 ± 2 mgm. for the group control (without follicle-stimulating hormone injections)

The qualitative response to the hormone was the same in both groups treated with follicle-stimulating hormone. The observation that ethylene dibromide did not affect the follicle-stimulating hormone *in vitro* supports the assumption that ethylene dibromide does not act on follicle-stimulating hormone directly, but attacks rather the formation or release of the hormone from the pituitary.

I am indebted to Prof. W. McShan, University of Wisconsin, for his interest in the work, helpful discussion and gift of the follicle-stimulating hormone preparation.

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[1] Olomucki, Eugenia, and Bondi, A., *J. Sci. Food and Agric.*, **6**, 592 (1955).
[2] Bondi, A., Olomucki, Eugenia, and Calderon, M., *J. Sci. Food and Agric.*, **6**, 600 (1955).
[3] Aman, T., Farkas, L., Ben-Shamai, M. H., and Plaut, M., *Ann. App. Biol.*, **33**, 389 (1946).
[4] Rowe, V. K., Spencer, H. C., McCollister, D. D., Hollinsworth, R. L., and Adams, E. M., *Arch. Ind. Hyg. Occup. Med.*, **6**, 158 (1952).
[5] McShan, W. H., Kagawa, C. M., and Meyer, R. K., *Proc. Soc. Exp. Biol. Med.*, **85**, 393 (1954).

Clearance of Injected Heparin from the Blood

HEPARIN is an extremely potent inhibitor of blood coagulation, and it is on the basis of this property that it has been widely accepted in the clinical treatment of thrombosis[1]. It is a sulphur-containing mucopolysaccharide which is naturally present in a number of animal tissues, the highest concentration being found in liver and lung[2] and very minute amounts in the blood[3]. When heparin is injected into the bloodstream, its anticoagulant activity manifests itself immediately ; however, this effect is lost within a comparatively short period of time. The problem as to the fate of the administered heparin and its concentration in blood at different intervals after injection is therefore of considerable importance from a pharmacological and physiological point of view. Previous studies on the metabolism of heparin presented some difficulty, since the concentrations involved were minute and the possibility always existed of contamination by other sulphated mucopolysaccharides. The preparation in this laboratory of heparin labelled[4] with sulphur-35 opened the possibility for tracing and quantitatively determining minute amounts of heparin in various tissues. The present communication is a report on the determination of heparin in blood subsequent to its administration as the labelled product. The correlation is shown between this concentration and the clotting time.

Dogs weighing 14·5 kgm. were injected intravenously with 30 mgm. sodium heparin-^{35}S having a specific activity of 8,200 c.p.m. per mgm. Clotting times by the Lee and White method[5] were determined on blood drawn at different intervals after administration. Simultaneously, radioactivity assays were made on 4-ml. blood samples by combustion and counting as barium sulphate[6].

Fig. 1 shows the results obtained in these experiments. The initial radioactivity immediately after

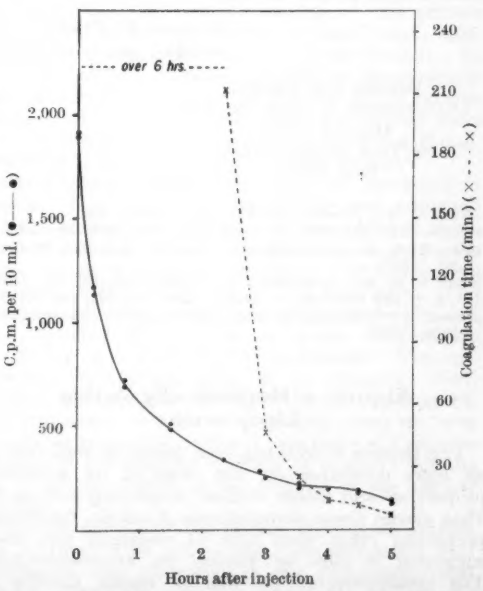

Fig. 1. Radioactivity in blood and coagulation time following injection of 30 mgm. of labelled heparin into 14·5-kgm. dogs

injection is 1,900 c.p.m. per 10 ml. of blood. This corresponds to 0·023 mgm. of heparin per ml. The clotting time of this blood was more than 24 hr. and consequently no accurate estimation could be made. During the first ½ hr. there is a sharp drop in the blood heparin concentration so that after 45 min. the radioactivity indicates that there are only 0·008 mgm. of heparin in each ml. Afterwards, the rate of removal of heparin from the blood decreased sharply so that after 3 hr. the concentration was still 0·003 mgm. per ml. The clotting time, on the other hand, became measurable only 2·7 hr. after injection and gave a normal value after 5 hr. At this time there were only traces of the injected heparin in the bloodstream.

Experiments were also conducted where 20, 40 and 50 mgm. of heparin were injected to dogs of similar weight. Although there is a prolongation in the physiological effects with increasing dosage, it was not considerable in the cases where more than 30 mgm. were administered. Radioactivity assay of the blood after different intervals indicated that the rate of elimination from the blood is greatest during the first 45 min. The rate of this ejection from the bloodstream increases as the dose administered is increased until the concentration is approximately 0·01 mgm. per ml.

These experiments also suggest that the comparatively rapid return of the bloodstream to normal is not due to any deactivation of the heparin within the bloodstream but to its rapid elimination as shown by the disappearance of radioactivity from the blood. Other studies indicate (unpublished results) also that heparin is not desulphated in the blood so that the loss of radioactivity is not due to the removal of the label from the tagged molecule. Thus the loss of the heparin effect is a result of the actual elimination of the molecule from the bloodstream.

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[1] Jorpes, J. E., "Heparin" (Oxford Univ. Press, 1946).
[2] Charles, A. F., and Scott, D. A., *J. Biol. Chem.*, **102**, 431 (1933).
[3] Eiber, H. B., and Danishefsky, I., *Proc. Soc. Exp. Biol. Med.*, **4**, 801 (1957).
[4] Eiber, H. B., and Danishefsky, I., *J. Biol. Chem.*, **226**, 721 (1957).
[5] Lee, R. I., and White, P. D., *Amer. J. Med. Sci.*, **145**, 495 (1913).
[6] Aronoff, S., "Techniques of Radiobiochemistry" (Iowa State Coll. Press, 1956).

Elastin, a Metabolically Active Lipoprotein

The protein elastin has been generally regarded as an inert substance on the basis of its solubility properties[1] and tracer studies[2] employing carbon-14. That elastic tissue demonstrates dynamic, functional properties other than that of elasticity has been suggested in part by studies on arteriosclerotics. The breakdown of the arterial elastic lamellæ is generally reported to be the initial event in the pathological changes of the arteries[3]. That the elastic lamellæ of arteries act as selective filters to tissue fluid components has been proposed[4]. The present report demonstrates that elastin, as it exists *in situ* in elastic tissue, is composed of metabolically active components.

Several reports have indicated that lipids affect the reactivity of elastin to the proteolytic enzyme, elastase, and Lansing has suggested that elastin is a lipoprotein[5-7]. In this laboratory elastin was prepared by conventional methods from beef ligamentum nuchæ and then exhaustively extracted for lipids over a period of several days. In the defatted protein a plasmalogen and unsaturated lipid were detected by means of the Schiff reaction. When defatted elastin was hydrolysed by elastase, extraction of the protein solution yielded a Schiff-positive unsaturated fatty compound the reactivity of which was blocked by bromination. Unsaturated fatty acids are known to react with Schiff's reagent, and Rapport and Franzl[8] have shown that certain aldehydes depend upon unsaturation in the molecule for their Schiff positivity. The amount of this lipid material in defatted elastin was estimated at 0·5 per cent of the dry weight.

The identification of protein-bound unsaturated fatty acid in elastin described above may well explain certain reported observations of other workers. Partridge and Davis[9] observed in elastolysates an unknown substance with an absorbance peak at 2750 A., which is in accord with the absorbance peaks due to the ethylenic bonds in unsaturated fatty acids. Balo and Banga[10] observed that a bromine-consuming substance was slowly released from a solution of elastin which was allowed to stand for several days. The bromine consumption was not due to liberated end groups, and the substance combining with bromine was dialysable. In this laboratory it was found that the unsaturated lipid in elastin was partially released during enzymatic hydrolysis. The findings of Balo and Banga may be explained upon a continued liberation of unsaturated lipid from the deteriorating soluble elastin. Elastin contains a yellow pigment, and a coloured solution results upon hydrolysis of the protein. The pigment cannot be removed either from the native sclero-protein or its soluble products. Kendall[11] observed a yellow pigment in a preparation of serum albumin which could be removed by lipid solvents only after denaturation of the protein. The substance was identified as an unsaturated fatty acid. The yellow substance in elastin is more tightly bound, since it is not extractable after the solubilized protein is boiled.

Plasmalogens have been reported to be lipid-soluble substances. That present in elastin is not extractable with fat solvents either from the insoluble sclero-protein or its soluble products, although it may be a tightly bound lipid. Partridge and Davis postulated the presence of a compound which is involved in the cross-linking of the polypeptide chains in elastin, since the known types of cross-linkages are not operative. The plasmalogen in conjunction with the protein-bound fatty acid may be concerned with this cross-linking.

That lipids are important in determining the integrity of elastic fibres is established by certain metabolic studies. Boucek and Noble[12] found that the scleroprotein of connective tissue incorporates lipid at a significant rate. Menschik[12] observed

fragmentation of cardiac elastic fibres in cases of vitamin E deficiency, the condition being aggravated by feeding unsaturated fatty acid or by eliminating saturated acids from the diet. Sinclair[14] showed that the formation of the polyunsaturated, essential fatty acid, arachidonic acid, from linoleic is mediated by vitamin B_6, and Rhinhart[15] has produced arteriosclerosis in monkeys made deficient in this vitamin.

I suggest that the non-extractable plasmalogen and unsaturated lipid found in the elastic protein are concerned with the maintenance of the elastic fibre. It is proposed that breakdown of the elastin molecule occurs when a deficiency in the normal lipid constituents occurs or when the constituent lipids are displaced by other lipids as a result of some metabolic lesion. For example, a high dietary intake of saturated fatty acid may result in the replacement of elastin-bound, unsaturated fatty acid by saturated fatty acid. The saturated acid–elastin complex is unstable, resulting in the degradation of the lipoprotein molecule. The breakdown of the elastic lamellæ then leads to lipid infiltration, plaque formation, and necrosis. Peifer[16] fed individual fatty acids in high concentrations to animals and found that the more saturated the acid the more diffuse were the arteriosclerotic lesions produced.

In addition to non-extractable, protein-bound fatty acid and plasmalogen, elastin contains about 0·01 per cent phosphorus which is resistant to extraction by cold acid, fat solvents, and hot 0·1 *N* alkali and is presumed to be in phosphoprotein combination. Radioactive studies in which phosphorus-32 was employed showed that the protein-bound phosphorus turns over at a rate second only to inorganic phosphorus. The specific activity of protein phosphorus in aortic elastin ranged from 10 to 25 per cent of the values for the specific activity of aortic inorganic phosphorus; the specific activities of lipid phosphorus and alkali-soluble phosphorus in the aorta were only 1 to 10 per cent of the values for inorganic phosphorus. Johnson and Albert[17] believe that phosphoprotein is not a storage form of phosphorus, since it is present usually in small concentrations, but that it may serve an enzymic function.

Reports in the literature in which carbon-14 was employed did not indicate the metabolic activity of the protein phosphorus component or of lipids which may be physically bound to elastin. Also, the carbon-14 activity of lipids in chemical combination with elastin would be masked by the greater proportion of the relatively inert protein carbon. Elastic tissue must be regarded as a whole rather than assigning to it a metabolic role which is the sum of its components. In conjunction with lipids, the active elastic lamellæ may well possess the function of a selective filter. In this laboratory significant concentrations of cerebroside have been determined in the ligamentum nuchæ and a functional, rather than a structural, role is suggested for this lipid, since it is found in relative paucity in the body.

The hypothesis is set forth that the elastic protein is a lipoprotein and more metabolically active than heretofore regarded. It is believed that the combination of the elastic protein with other substances, as described above, possesses distinct characteristics, both chemical and physical, which none of the components demonstrates alone. It is further suggested that unsaturated fatty acid is essential for maintaining the integrity of the fibrous protein. Qualitative or quantitative alterations in body lipids, as produced by dietary or pathological states, affect the type of scleroprotein–lipid complex and hence the state of the elastic fibre. The arteriosclerotic events generally initiated by elastic-tissue degradation may well be due primarily to a biochemical lesion in lipid metabolism. Studies to test these hypotheses further are being undertaken.

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[1] Stein, W. H., and Miller, E. C., jun. *J. Biol. Chem.* **125**, 599 (1938).
[2] Slack, H. G. B., *Nature*, **174**, 512 (1954).
[3] Blumenthal, H. J., *et al.*, *Amer. J. Path.*, **26**, 989 (1950).
[4] Gross, J., Symposium on Atherosclerosis, Nat. Res. Coun., Washington, p. 41 (1954).
[5] Findlay, G. H., *Brit. J. Dermat.*, **66**, 16 (1954).
[6] Laszlo, J., and Schuler, D., *Acta Physiol. Acad. Sci. Hung.*, **6**, 463 (1954).
[7] Lansing, A. I., Trans. Macy Conf. on Connective Tissue, **2**, 45 (1951).
[8] Rapport, M. M., and Franzl, R. E., *J. Biol. Chem.*, **225**, 851 (1957).
[9] Partridge, S. M., and Davis, H. F., *Biochem. J.*, **61**, 21 (1955).
[10] Banga, I., and Balo, J., *Acta Physiol. Acad. Sci. Hung.*, **6**, 235 (1954).
[11] Kendall, F. E., *J. Biol. Chem.*, **138**, 97 (1941).
[12] Boucek, R. J., and Noble, N. L., *Circ. Res.*, **5**, 27 (1957).
[13] Menschik, Z., *Anat. Rec.*, **124**, 333 (1956).
[14] Sinclair, H. M., *Lancet*, i, 386 (1956).
[15] Rhinehart, J. F., "Connective Tissue in Health and Disease", edit. Asboe-Hansen G., p. 239 (Munksgaard, Copenhagen, 1954).
[16] Peifer, J. J., *Fed. Proc.*, **16**, 232 (1957).
[17] Johnson, R. M., and Albert, S., *J. Biol. Chem.*, **200**, 335 (1953).

Composition of Muscle in Malnourished Human Infants

ALTHOUGH protein deficiency is probably the commonest form of malnutrition throughout the world, there is no means of assessing its severity in the living subject. One approach to this problem is by tissue analysis. Measurement of the protein content of tissues by itself is of little value, since significant changes do not seem to be found[1]. If, however, protein content is related to deoxynucleic acid, an index is obtained of the amount of protein per cell. By this method we have shown that there is a very severe loss of protein from the livers of malnourished infants on a protein-deficient diet[2].

These measurements have now been extended to muscle. 7–10 days after the infants were admitted to hospital, samples of muscle weighing 50–100 mgm. were taken under local anæsthesia from m. pectoralis major in the anterior axillary fold. The biopsy was repeated on the other side 1–3 months later. The tissue was dried *in vacuo* over calcium chloride, and then digested for 48 hr. at room temperature (~ 30° C.) in 0·5 *M* lithium hydroxide. The undissolved residue was taken to be collagen. Non-collagen nitrogen was measured in the supernatant. It is important to allow for collagen, since we have found that in protein-depleted rats there is a relative increase in the collagen content of muscle; all the loss of protein occurs at the expense of the cellular fraction[3].

Another aliquot of the lithium hydroxide extract was acidified with nitric acid. Deoxynucleic acid phosphorus was measured in the precipitate, and sodium, potassium, chloride and total phosphorus in the supernatant. This supernatant phosphorus

Table 1. Composition of Muscle in Eighteen Malnourished Infants

	First biopsy	Second biopsy	Significance of difference : P
Body-weight, per cent of ideal weight	53*	68·5	
Non-collagen nitrogen, mgm. per mgm. deoxynucleic acid phosphorus	237 ± 16·5	343 ± 15·2	< 0·01
Potassium, μeq. per mgm. non-collagen nitrogen	2·43 ± 0·074	2·82 ± 0·08	< 0·01
'Supernatant' phosphorus, μgm. per mgm. non-collagen nitrogen	26·3 ± 1·57	32·3 ± 1·95	0·05
Water content, per cent	77·6 ± 0·053	75·7 ± 0·063	< 0·05 > 0·01
Sodium, μeq. per 100 mgm. dry weight	33·4 ± 1·44	27·6 ± 1·81	< 0·05 > 0·01
Sodium/chloride, μeq. per μeq. (whole muscle)	1·42 ± 0·073	1·365 ± 0·080	not significant
	Mean, ± standard error		

* Body-weight was measured after the loss of clinical œdema

fraction includes inorganic phosphate, acid-soluble phosphate esters and ribonucleotides.

The results in eighteen consecutive cases are shown in Table 1. Between the first and second biopsies, the ratio non-collagen nitrogen/deoxynucleic acid phosphorus increased by 45 per cent. On the assumption that the pectoral muscle is representative of the musculature as a whole, this figure gives a minimum estimate of the increase in muscle mass. If, as is probable, new deoxynucleic acid was formed as well as new protein, then the increase in muscle mass would be more than 45 per cent.

The increase in body-weight during this period was not so great—only 29 per cent. The discrepancy can be explained by the suggestion, often made but never proved, that during recovery the gain in tissue protein is partially masked by loss of water and of fat. Further evidence is provided by the fact, observed by us and by others, that in the early stages of recovery nitrogen balances are positive, with little or no increase in body-weight[4].

The normal ratio of potassium/nitrogen in muscle is 3 ; it was unexpected to find the ratio still low at the time of the first biopsy, since this was not done until treatment had been given for the acute disturbances of water and electrolyte balance that are often present when the infant first comes to hospital[5].

The reduction in 'supernatant phosphorus' was somewhat variable, but in the group as a whole was significant. Balance studies also point to a phosphorus deficiency ; some infants in the early stages of recovery retain large amounts of phosphorus, and excrete practically none in the urine.

The water-content of the muscle and the sodium content were slightly increased at the time of the first biopsy, even though this was not done until clinical œdema had disappeared. It is probable that these increases were in the extracellular phase, since the ratio of sodium/chloride was not significantly different in the initial and final specimens.

We are indebted to Miss V. G. Wills, who performed the biopsies.

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[1] Holmes, E. G., Jones, E. R., Lyle, Margaret, D., and Stanier, Margaret W., *Brit. J. Nutr.*, **10**, 198 (1956).
[2] Waterlow, J. C., and Weisz, T., *J. Clin. Invest.*, **35**, 346 (1956).
[3] Mendes, C. B., and Waterlow, J. C. (to be published).
[4] Protein Malnutrition, Proc. Conf., convened in Jamaica by the Food and Agriculture Organization of the United Nations, the World Health Organization and the Josiah Macy, Jr. Foundation, edited by J. C. Waterlow (FAO, Rome, 1955).
[5] Hansen, J. D. L., and Jenkinson, V., *S. Afr. J. Lab. Clin. Med.*, **2**, 205 (1956).

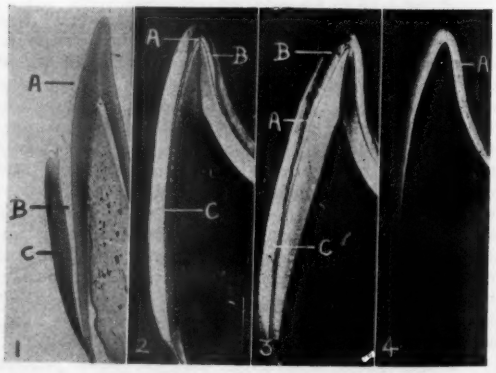
Mineralization of Human Enamel

Since the publication in 1940 of Diamond and Weinmann's work on amelogenesis[1], there has been, with a few exceptions[2–5], widespread support for their views on enamel mineralization. The findings of a recent investigation in this laboratory, however, show that the later stages of mineralization of the enamel do not occur as outlined in the Diamond and Weinmann theory.

In this investigation human deciduous teeth ranging in age from 26 weeks *in utero* to 18 months postnatal were examined. The appearances of routinely decalcified sections were correlated with the microradiographic and the polarized light appearances of ground sections from the same teeth. The following results, obtained with a deciduous maxillary first incisor from a two-weeks postmature infant, illustrate these findings.

The tooth was dissected from its follicle, fixed in 10 per cent formol-saline and bisected longitudinally labio-lingually. From the mesial half thus obtained a 100-μ thick ground section was prepared. Decalcified sections (using a formic and citric acid mixture) were prepared from the distal half of the same tooth.

The ground-section, when immersed in distilled water ($n = 1{\cdot}335$) and studied in plane polarized light, showed a thin zone of enamel of negative intrinsic birefringence along the incisal part of the amelodentinal junction, broadening out on its lingual side (Fig. 2). In potassium mercuric iodide ($n = 1{\cdot}47$) this area of negative birefringence had expanded



Figs. 1–4. 1, Decalcified section from distal half of a deciduous maxillary central incisor (× 8·5); *A*, Area of 'soluble' enamel matrix ; *B*, artefact space ; *C*, 'insoluble' enamel matrix. 2, Ground-section from mesial half of same tooth as (1), in water ; polarized light (× 7·5). *A*, negatively birefringent enamel ; *B*, isotropic enamel ; *C*, positively birefringent enamel. 3, Same section as 2, but in potassium mercuric iodide ; polarized light (× 7·5). *A*, negatively birefringent enamel ; *B*, isotropic enamel ; *C*, positively birefringent enamel. 4, Microradiograph of same section as 2 (× 7·5). *A*, Lingual area of highest X-ray absorption

cervically along the full length of the amelo-dentinal junction, and peripherally to the enamel surface on the lingual side of the incisal region (Fig. 3). A microradiograph of the same ground section showed high absorption along the amelo-dentinal junction broadening out in the lingual incisal area (Fig. 4).

The polarized light and microradiographic observations thus showed that the later stages of enamel mineralization started at the incisal amelo-dentinal junction and expanded peripherally and cervically in a plane neither parallel nor perpendicular to the striæ of Retzius.

The decalcified sections, however, showed the line of junction between the 'soluble' and the 'insoluble' enamel organic matrix to be at right angles to the striæ of Retzius (Fig. 1).

This result, which is clearly in conflict with the X-ray and polarized light findings, indicates on the Diamond and Weinmann theory a secondary mineralization direction at right angles to the striæ of Retzius.

As the X-ray absorption under the experimental conditions used was almost entirely due to the mineral matter present, it may be assumed that the microradiograph accurately recorded the distribution of mineral matter and hence the direction of mineralization. This distribution was further confirmed by the variations in the sign and strength of birefringence shown in polarized light.

The decalcified sections, however, gave direct information concerning only the enamel organic matrix, not the mineral matter.

These results therefore suggest that the sequence of changes in 'solubility' of the enamel organic matrix does not occur in exactly the same direction as the later stages of mineralization, and is of limited value in assessing the extent and direction of the latter.

A full account of this work will be published later.

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[1] Diamond, M., and Weinmann, J. P., "Enamel of the Human Teeth" (Columbia Univ. Press, New York, 1940).
[2] Saunders, J., Nuckolls, J., and Frisbie, H. E., *J. Amer. Coll. Dent.*, **9**, 107 (1942).
[3] Nuckolls, J., Leicester, H. M., and Dienstein, B. J., *J. Amer. Coll. Dent.*, **14**, 118 (1947).
[4] Hals, E., "Fluorescence Microscopy of Developing and Adult Teeth" (Norwegian Academic Press, Oslo, 1953).
[5] Engfeldt, B., and Hammarlund-Essler, E., *Acta Odont. Scand.*, **14**, 273 (1956).

Use of Logarithms to the Base 2 in recording Serological Reactions

The expression of dilution titres for serological reactions frequently requires the use of large numbers. In cases where the antibody content of an immune serum is high, the conventional means of recording the titre may be misleading; that is, the difference between a titre of 1 : 10,240 and 1 : 20,480 seemingly is greater than that between 1 : 40 and 1 : 80 but both represent only a single dilution step in the usual procedure and have the same degree of precision. Since serological procedures usually involve serial two-fold dilutions, the resulting titres are exponential functions of 2. Consequently, we suggest the simple expedient of using logarithms to the base 2 ($\log_2$) to express serological titration data.

A convenient table of logarithms to the base 2 has recently been published[1], and conversion from $\log_{10}$ values is readily made from the relationship,

$$\log_2 n = 3{\cdot}322 \log_{10} n$$

In a serological dilution series of 1 : 2, 1 : 4, 1 : 8, 1 : 16 . . . 1 : 2^n, the resulting $\log_2$ values follow directly as 1, 2, 3, 4 . . . n. In a series in which the initial dilution is other than 1 : 2, it is a simple matter to add to the subsequent 2^n dilution series the $\log_2$ of that initial dilution; for example, in a dilution series of 1 : 10, 1 : 20, 1 : 40, 1 : 80 . . . 1 : 10 × 2^n, the resulting $\log_2$ values are 3·32, 4·32, 5·32 . . . 3·32 + n.

Although titrations of antiserum still are commonly made by serial two-fold dilutions, greater precision may be obtained by using smaller dilution steps. This superior principle has been applied by Horsfall and Tamm[2] using a fractional dilution procedure in steps of 0·1 $\log_{10}$ unit, in which case the titres may be expressed as common logarithms.

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July 22.

[1] Finney, D. J., Hazelwood, T., and Smith, M. J., *J. Gen. Microbiol.*, **12**, 222 (1956).
[2] Horsfall, F. L., and Tamm, L., *J. Immunol.*, **70**, 253 (1953).

Selectively Balanced Polymorphism at a Sex-linked Locus

A stable selectively balanced polymorphism dependent on a pair of autosomal genes (or chromosomal arrangements) is known to exist when the heterozygote is at a selective advantage with respect to both homozygotes. It has sometimes been assumed[1] that the same conditions apply also to a selectively balanced polymorphism at a locus in the X-chromosome and that the existence of heterosis may consequently be inferred when heterozygotes are found to be more frequent than homozygotes in the homogametic sex. However, these assumptions seem to be unwarranted.

We must take account of the relative selective values of the different genotypes in both sexes. If there are two allelomorphs A and a at a given locus in the X-chromosome, there are two genotypes in the heterogametic sex (which we shall assume to be male) one containing the gene A and the other a. Let the selective values of these two genotypes be in the ratio $t_A : 1$, where $t_A = 1 + h$, say, will be taken to be greater than one. In the homogametic sex there are three genotypes, AA, Aa and aa, and we shall suppose that their selective values are in the ratio $S_{AA} : 1 : S_{aa}$. It can be shown that the gene ratio can have a stable equilibrium value if and only if $S_{aa} < 1 + \frac{1}{2}h$ and $S_{AA} < 1 - \frac{1}{2} \cdot \frac{h}{1+h}$. The equilibrium value of the gene ratio in the gametic output of females is then :

$$\left(\frac{p_A}{p_a}\right)_f = \frac{1 + t_A - 2S_{aa}}{1 + t_A - 2t_A.S_{AA}}$$

while in males it is:

$$\left(\frac{p_A}{p_a}\right)_m = t_A \cdot \left(\frac{p_A}{p_a}\right)_f$$

Clearly, when t_A has any value other than unity, it is neither necessary nor sufficient for the heterozygote to be at a selective advantage with respect to both homozygotes in order that a stable balanced polymorphism may exist. Thus, for example, when $t_A = 1{\cdot}5$, and $S_{AA} = 0{\cdot}8$, $S_{aa} = 1{\cdot}1$, there is a stable equilibrium value for the gene ratio, but when $t_A = 1{\cdot}5$ and $S_{AA} = S_{aa} = 0{\cdot}9$, no equilibrium exists.

Not only is heterosis in the homogametic sex neither necessary nor sufficient for the existence of a selectively balanced polymorphism at a sex-linked locus but also the occurrence of heterozygotes with a frequency in excess of that of homozygotes is not necessarily an indication of the existence of heterosis at such a locus. As an example showing a marked excess of heterozygotes in the absence of heterosis, we may take the case where $t_A = 6$, $S_{AA} = \frac{1}{3}$ and $S_{aa} = 2$; 64 per cent of adult females in such a population will have the genotype Aa when equilibrium is attained.

Several examples of polymorphism at sex-linked loci are being investigated in this Laboratory with the view of comparing a range of observational data with the above results.

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[1] da Cunha, A. B., *Nature*, **172**, 815 (1953).

Induction of Translocations in Mice by Triethylenemelamine

The findings of Jackson and Bock[1] that triethylenemelamine causes male sterility in rats instigated an investigation into the possibility that this effect is at least partially due to the production of dominant lethals through chromosome breakage. If this were true, one might expect to find that a proportion of the survivors carry translocations. In support of this idea is the work of Fahmy and Fahmy[2,3] on *Drosophila*, where it was shown that triethylenemelamine induces a high frequency of translocations as well as dominant lethals. A search for translocations in the offspring of treated male mice was therefore started.

Two groups of mice were treated, one group being composed of five males (Exp. 1) and the other group of sixteen males (Exp. 2). The method of treatment was the same in both cases: it consisted of two intraperitoneal injections of solutions of triethylenemelamine on two consecutive days. The solutions were made up with 0·9 per cent sodium chloride and the doses used were 0·8 mgm./kgm. in Exp. 1 and 0·64 mgm./kgm. in Exp. 2. The Exp. 1 males were mated to unrelated females throughout the week following treatment, but litters were only produced to matings within the first two days. Such litters as were born ranged in size from one to four; consequently only twelve F_1 animals in all were produced and could be tested. These consisted of nine females and three males. In Exp. 2, the males were each placed with five unrelated females after treatment and allowed to mate at random. Litters were only produced to matings in the first five days after the second injection; thereafter no progeny were produced until the twelfth day. Seven males and two females from the early litters and also nine males from the later litters were tested.

It has been shown that a proportion of the progeny of X-irradiated male mice produce small litters when mated to normal animals, and this defect re-occurs in about half their progeny. This condition has been called heritable semi-sterility[4,5] or heritable partial sterility[6]. Snell[7,8] has genetically proved that such animals are heterozygous for a reciprocal translocation, and this has been confirmed cytologically by Koller[9,10]. In the present experiments, suspected heterozygotes for a translocation were selected on the basis of litter size. The males were then tested cytologically by the method described by Slizynski[11,12], where it can be seen that such heterozygotes regularly show nineteen instead of twenty tetrads at diplotene, diakinesis, and metaphase of the first meiotic division. Both the genetical and cytological methods for detecting translocations give less conclusive results in females than in males; small litters may be due to physiological rather than genetical causes, and good cytological pictures are much more difficult to obtain. Females suspected of being semi-sterile were therefore tested by their sons. A female which carries a translocation will transmit this property to about half her sons; these will be semi-sterile and can be examined cytologically for the presence of a translocation.

The following results were obtained. In Exp. 1, eight out of twelve F_1 animals were normal as judged by the size of their litters. These were discarded without further tests. Two females had small litters and were shown to carry a translocation by tests on their sons. A third female was suspected of being semi-sterile, for she produced only one litter of a single offspring which died at an early age. Finally, one male was suspected of being completely sterile, for before suddenly dying of some unknown cause, he had access for two weeks to females which did not produce any litters afterwards. In Exp. 2, only one F_1 male was judged normal by the size of his litters. Of the remaining six males, two were heterozygous for a translocation, and four (two by the same treated father) were completely sterile. Both females produced small litters, and the examination of their sons showed that they were heterozygous for a translocation. The nine males from the later litters all produced normal litters except one, which was completely sterile. This male had been sired by the same treated animal which produced two sterile sons in the early litters. Cytological examination of the sterile males showed that only one carried a translocation. In all these males, spermatogenesis proceeded to pachytene or metaphase of the first meiotic division, but only one produced a very small number of spermatozoa, and these were grossly abnormal. It seems that this type of complete sterility is caused, not by multiple translocations but by a breakdown of spermatogenesis which may or may not proceed far enough to produce abnormal sperm. The ultimate cause of this phenomenon may be a dominant mutation.

When the results of Exps. 1 and 2 are combined, there are six or possibly seven semi-sterile animals out of the twenty-one tested, that is, 28·5 or 33·3 per cent. This is about the same frequency of translocations as is produced by a dose of 600 r. X-rays. At equivalent doses, the number of completely sterile animals produced by triethylenemelamine seems higher than that produced by X-rays. Russell[6] quotes a figure of 10 per cent dominant sterility for 700 r. X-rays as compared with 19 per cent produced by triethylenemelamine. The fact that a completely sterile F_1 animal, with similar defects in spermatogenesis, occurred in a later litter, might seem to indicate another difference from irradiation, which rarely leads to the production of sterile 'Spätprobanden'. However, since the early sterile period after treatment with triethylenemelamine is probably a different phenomenon from the later one caused by X-rays, such a comparison may not be valid.

Triethylenemelamine is a powerful chemical mutagen for mice, much more powerful than nitrogen mustard[12], which produced only a few translocations at doses which were highly toxic. It will be interesting to study the efficiency of triethylenemelamine in producing other types of genetical change.

I would like to thank Dr. C. Auerbach and Dr. B. M. Slizynski for most helpful advice and criticism, and also Prof. C. H. Waddington for laboratory facilities. I acknowledge a grant from the Agricultural Research Council.

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[1] Jackson, H., and Bock, M., *Nature*, **175**, 1073 (1955).
[2] Fahmy, O. G., and Fahmy, M. J., *J. Genet.*, **52**, 603 (1954).
[3] Fahmy, O. G., and Fahmy, M. J., *J. Genet.*, **53**, 603 (1955).
[4] Hertwig, P., *Z. indukt. Abstammungs-u. Vererbungslehre*, **71**, 1 (1940).
[5] Snell, G. D., *Genetics*, **20**, 247 (1935).
[6] Russell, W. L., "Radiation Biology", **1**, Chap. 12 (McGraw-Hill, New York, 1954).
[7] Snell, G. D., *Genetics*, **26**, 169 (1941).
[8] Snell, G. D., *Genetics*, **31**, 157 (1946).
[9] Koller, P. C., *Genetics*, **29**, 247 (1944).
[10] Koller, P. C., and Auerbach, C., *Nature*, **148**, 501 (1941).
[11] Auerbach, C., and Slizynski, B. M., *Nature*, **177**, 376 (1956).
[12] Falconer, D. S., Slizynski, B. M., and Auerbach, C., *J. Genet.*, **51**, 81 (1952).

Relation of Structure of 2,4-Dichlorophenoxyacetate to its Mode of Action as an Auxin

Heath and Clark[1] have proposed a possible mechanism for the mode of action of auxin which involves interference with metal ion metabolism. This conclusion was based on work involving the growth stimulation of wheat coleoptile sections. They found a particularly interesting relationship between many known chelators of various molecular structure and their ability to act as growth substances. These workers extended their findings on this relationship of chelators and growth stimulation with root-growth experiments[2].

Almost simultaneously, Johnson and Colmer[3-5] proposed a mode of action for the commonly used herbicide 2,4-dichlorophenoxyacetate to explain its inhibition of the respiration of *Azotobacter vinelandii*. Their findings related the inhibitory action of 2,4-dichlorophenoxyacetate to its ability to chelate or produce complex formation with magnesium, an element well known for its essential role in the activity of cells[6,7].

The argument should be strengthened by the fact that both pairs of workers independently, and using two completely different approaches, arrived at the same conclusion.

Plant physiologists and workers in chemical weed control have reported on many studies dealing with the specificity of the structure of 2,4-dichlorophenoxyacetate and its related compounds to their toxicity for plants. Since our work with 2,4-dichlorophenoxyacetate related its toxicity to its ability to deny magnesium to the cell, it was thought to be of interest to study the interaction of some related compounds on the magnesium content of the environment of the test bacterium.

The organism used was *A. vinelandii* strain *O*. The nitrogen-free mineral salts solution of Burk[8] with 1 per cent mannitol was the growth medium. The organisms were grown in 300 ml. of medium in a 1,000 ml. flask on a rotary-type shaker at 30 C.° for 16–18 hr.

At the end of the growth period the cells were centrifuged from the medium at 3,000 r.p.m. for 10 min. at 4° C. The cells were washed and centrifuged once with 10 ml. amounts of 0·2 per cent potassium chloride solution, *p*H 6·9. They were suspended in 0·2 per cent potassium chloride and filtered through Reeve Angel filter paper No. 202, and were then adjusted to an optical density of 1·0 with a B. and L. Spectronic 20 spectrophotometer at 420 mμ.

The usual Warburg procedures were employed[9]. Each flask had in the reaction chamber the following materials expressed as final molar concentrations in a total volume of 2·5 ml.: cells, 0·5 ml.; phosphate buffer *p*H 6·9–7·0, 0·08 *M*; magnesium sulphate, and the test compounds as indicated. The side-arms of the flasks had 0·1 ml. of a 0·1 *M* solution of mannitol which when tipped gave a final concentration of 0·003 *M*. The centre well had 0·1 ml. of 10 per cent potassium hydroxide and a fluted filter paper strip. All vessels were made to volume with triple-distilled water.

The gas phase was air and the temperature was 31° C. The vessels were allowed to equilibrate for 5 min. and then the substrate was tipped in from the side-arms. Oxygen uptake was measured for 60 min. The 2,4-dichlorophenoxyacetate used was obtained from the Dow Chemical Co. and was labelled 'pure'. All the other compounds were purchased from the Eastman Kodak Co.

Table 1 shows that phenoxyacetate, lacking chlorine atoms, is much less toxic to *A. vinelandii* than 2,4-dichlorophenoxyacetate. Phenylpropionate lacking both chlorine atoms and the oxygen of phenoxy-

Table 1. Relationship of Structure of 2,4-Dichlorophenoxyacetate and Related Compounds to their Inhibition of Respiration of *A. vinelandii*

Agents	Concentration for complete inhibition of respiration of *A. vinelandii*	Molar ratio of magnesium to agent for complete protection from this inhibition
2,4-Dichlorophenoxyacetate	8×10^{-5} *M*	1 : 1
Phenoxyacetate	2×10^{-3} *M*	1 : 1
Phenylpropionate	2×10^{-3} *M*	2 : 1
ortho-Chlorophenoxyacetate	2×10^{-3} *M*	2 : 1
para-Chlorophenoxyacetate	1×10^{-3} *M*	1 : 1

acetate but having the same side-chain length also was less toxic than 2,4-dichlorophenoxyacetate. The position of the chlorine atom on the ring structure of the test compound altered the toxicity of it as shown when the *ortho* or *para* configuration was used. It was only when 2,4-dichlorophenoxyacetate with its specific configuration was used, however, that the greatest toxicity was demonstrated. These findings concerning molecular structure and activity agree with those of Zimmerman and Hitchcock[10] in their work with higher plants.

Table 1 also shows that in all cases the inhibiting action of the test agents was abolished by the addition of low molar ratios of magnesium to the agents. These low ratios are of particular interest in light of the findings of Soncin[11]. In his tests with certain tetracyclines and *Escherichia coli* a molar ratio of 50,000 : 1 magnesium to the test agent was needed to prevent inhibition.

The work reported here with the synthetic auxin 2,4-dichlorophenoxyacetate and its relation to the essential element magnesium in the respiration of the test bacterium lends emphasis to the explanation of Heath and Clark that a possible mode of action of auxin is the chelation or complexation of metal ions.

This work was made possible in part by a grant from the Southern Fellowships Fund to one of us (E. J. J.).

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[1] Heath, O. V. S., and Clark, J. E., *Nature*, **177**, 1118 (1956).
[2] Heath, O. V. S., and Clark, J. E., *Nature*, **178**, 600 (1956).
[3] Johnson, Emmett J., and Colmer, Arthur R., *J. Bacteriol.*, **73**, 139 (1957).
[4] Johnson, Emmett J., and Colmer, Arthur R., *J. Bacteriol.*, **73**, 666 (1957).
[5] Johnson, Emmett J., and Colmer, Arthur R., "Antibiotics and Chemotherapy" (in the press).
[6] Webb, M., *Science*, **118**, 607 (1953).
[7] Lehninger, A. L., "Harvey Lectures" (Academic Press, New York, 1953–54).
[8] Wilson, P. W., and Knight, S. G., "Experiments in Bacterial Physiology" (Burgess Publishing Co., Minneapolis, Minn., 1952).
[9] Umbreit, W. W., Burris, R. H., and Stauffer, J. F., "Manometric Techniques and Tissue Metabolism" (Burgess Publishing Co., Minneapolis, Minn., 1949).
[10] Zimmerman, P. W., and Hitchcock, A. E., *Contrib. Boyce Thompson Inst.*, **12**, 321 (1942).
[11] Soncin, E., *Arch. Int. Pharmacodyn et Therapie*, **94**, 346 (1953).

Starch-gel Electrophoresis of Animal Sera

Using a starch-gel electrophoresis technique[1], Ashton[3] investigated the serum protein patterns of the cow, dog, horse and pig. We have been using this technique for studying vitamin B_{12} binding by serum proteins. For comparative purposes, we have also examined the sera of various animal species. In this way we have obtained the starch-gel electrophoresis patterns which are shown in Fig. 1.

The differences between the species are well illustrated. In common with Ashton we have not actually identified the protein bands in different species. We have, however, run human and various animal sera concurrently on the same gel. A typical picture of such a gel with dog serum can be seen in

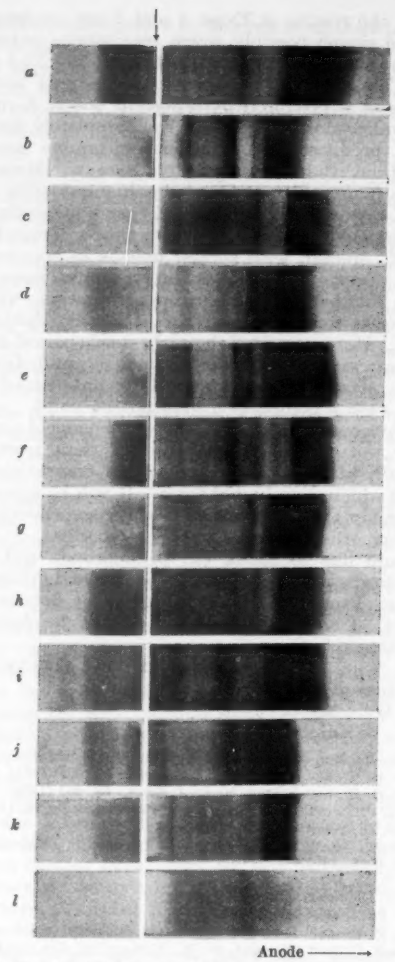

Fig. 1. Results of starch-gel electrophoresis of the sera of various animals: *a*, human; *b*, rat; *c*, mouse; *d*, guinea pig; *e*, rabbit; *f*, cat; *g*, dog; *h*, horse; *i*, cow; *j*, sheep; *k*, pig; *l*. cod. The top arrow indicates the position of the serum sample slot

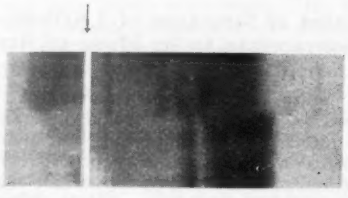

Fig. 2. Results obtained with human and dog sera run side by side on the same gel. The human serum is the upper

Fig. 2. This illustrates the fact that there is remarkably little correspondence in the relative intensity of the various bands of the two species. Also, there is not always correspondence in position of the bands. In the human the most intensely staining narrow bands are the fast alpha 2 ($F\alpha_2$), the beta and the slow alpha 2 ($S\alpha_2$). In the dog the only really intensely staining narrow band appears just in front of a fainter band travelling with the same electrophoretic mobility as human fast alpha 2.

It will be seen that a number of the bands do correspond in position, and for the time being for purposes of identification we propose to give similar designation as for the human to those bands with corresponding mobilities in animal sera.

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[1] Smithies, O., *Biochem. J.*, **61**, 629 (1955).
[2] Ashton, G. C., *Nature*, **179**, 824 (1957).

Cytochemical Localization of Acid Phosphatase in *Trichonympha turkestanica* Bernstein (Trichonymphina, Trichonymphidae)

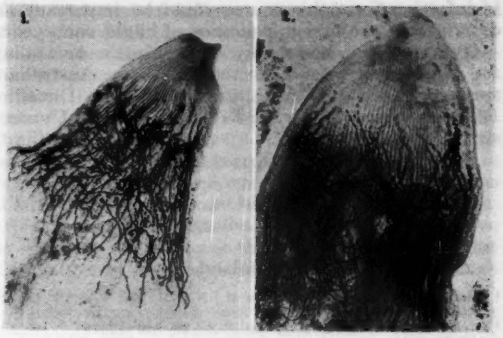
H. W. Dean and E. W. Dempsey[1] found prominent deposits of acid phosphatase in the Golgi region of the duodenal epithelium in the rat, mouse, deer mouse, hamster, cat and monkey. They also recorded the presence of well-defined concentrations of acid phosphatase in the Golgi zone of the uterine epithelium of the pregnant cat and sow. These two authors also observed granular deposits of the same enzyme in the Golgi region and in the apical cytoplasm of cells from the liver and kidney of sundry species.

Bourne[2] mentioned that the acid phosphatase of the intestinal mucosa occurs in the cytoplasm of the cells, particularly in the region occupied by the Golgi element.

In his work on the spermatogenesis of guinea pig, R. B. Sharma (unpublished work) pointed out that the acid phosphatase granules seem to follow, in a way, the fate of the Golgi apparatus. From the spermatogonia to the final formation of the sperm, the Golgi apparatus can be seen in the acid phosphatase preparations by the phase-contrast microscope. In the spermatogonia, the negative image of the Golgi apparatus was seen along the site of localization of the enzyme granules. Similarly, the negative image of the Golgi apparatus was visible in the spermatocytes and spermatids. He also added that the Golgi apparatus might secrete this enzyme, but he had no proof.

In the present work, I was able to demonstrate that the only organelle which shows any reaction to the acid phosphatase Gomori technique[3] in the protozoan *Trichonympha turkestanica* Bernstein is the parabasal apparatus (Figs. 1 and 2). *Trichonympha turkestanica* Bernstein is a symbiotic zooflagellate living in the lumen of the hind gut of the termite *Anacanthotermes ochraceus* (Burm.). This protozoan has a characteristic parabasal apparatus in the form of about fifty irregularly twisted cords that are relatively large. Each parabasal cord has a diameter of about 3 microns. Some of these cords may attain a length of about 100 microns. Pierre Grassé and Nina Carasso[4] showed by electron microscope studies that the parabasal apparatus of zooflagellates (*Trichonympha*, *Spirotrichonympha*, *Trimitus*, *Foania*, *Joenia*), the dictyosomes of somatic and germinal cells, and the Golgi 'cords' of secretory cells have the same composition and are strictly homologous elements.

The protozoan under investigation, with its conspicuous and characteristic Golgi apparatus



Figs. 1 and 2. Cytochemical reaction of acid phosphatase (Gomori's method) in *Trichonympha turkestanica* Bernstein. The incubation period is 1 hr. in Fig. 1 and 18 hr. in Fig. 2

(parabasal apparatus), is excellent material for showing the close relationship between the Golgi apparatus and the sites of localization of the acid phosphatase enzyme.

I thank Prof. J. Brontë Gatenby for suggesting and supervising this work.

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[1] Dean, H. W., and Dempsey, E. W., *Anat. Rec.*, **93**, 401 (1945).
[2] Bourne, G., "Cytology and Cell Physiology" (Clarendon Press, Oxford, 1951).
[3] Gomori, G., *Arch. Path.*, **32**, 189 (1941).
[4] Grassé, P. P., and Carasso, N., *Nature*, **179**, 31 (1957).

Infection of Native *Solanum* Species by the Potato Blight Fungus

Since the discovery of *Phytophthora infestans* (Mont.) de Bary on the New Zealand shrub *Solanum aviculare* Forst.[1] in native bush near Auckland by Miss J. M. Dingley, many other infected plants of this species have been found in both the North and South Islands (Brien, R. M., personal communication).

A sample of fungus from *S. aviculare* received in June 1956 was inoculated to leaves and tubers of a number of commercial potato varieties, to leaves of a series of differential hybrids, and to leaves of *S. aviculare* and the related species *S. laciniatum* Ait[2]. Susceptible varieties and the two native species were readily infected, but no hybrid carrying one or more immunity genes was infected, suggesting the presence[3] of the common race *O*. Blight spores were taken from *S. laciniatum* and inoculated to a further series of plants as above with the same result.

In May 1957 blight races 0, 1, 4, 1–3, 2–4, were isolated from samples collected throughout New Zealand. Both species were susceptible to all races. In June 1957 blight was found on plants of *S. laciniatum* growing in the Lincoln township, and tests indicate the presence of race *O*.

In the past, diseased tubers have been considered to be the sole means for carrying on the fungus from year to year. In New Zealand it would appear that these two shrubs could well act as overwintering hosts. Both species are common, *S. aviculare* mainly in the north and *S. laciniatum* in the south[2]. In view of the small foci needed to start an epidemic[4], and the distance spores can travel[5], even a small amount

of infection from this source could be important in determining the first appearance of blight each year.

Overwintering hosts may occur also in Australia, for blight has been collected from the Australian species, *S. simile* Muell., growing in the Dunedin Botanic Gardens by Dr. G. T. S. Baylis of the University of Otago (Brien, R. M., personal communication).

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[1] Brien, R. M., and Dingley, Joan M., *N.Z. J. Sci. Tech.*, A, **37**, 27 (1955).
[2] Baylis, G. T. S., *Trans. Roy. Soc. N.Z.*, **82**, 639 (1954).
[3] Black, W., Mastenbroek, C., Mills, W. R., and Peterson, L. C., *Euphytica*, **2**, 173 (1953).
[4] Hirst, J. M., *Plant Path.*, **4**, 2, 44 (1955).
[5] Van der Zaag, D. E., Dissertation, Wageningen (1956).

Water Absorption by Submerged Leaves

Dixon[1,2] and van der Paauw[3,4] have both recorded the uptake of water by the cut ends of submerged shoots of land plants; but there is divergence in their findings concerning the factors which affect the rate of absorption. Dixon found that factors which favoured rapid photosynthesis caused an increased rate of absorption. Van der Paauw found that in illuminated shoots the rate of water uptake was reduced to zero or that water was even exuded from the cut end, but darkness favoured absorption. Other workers[5] were unable to confirm Dixon's early results.

Recent work in this laboratory, on single cut leaves of *Bignonia grandiflora*, indicates that the pre-treatment of the material may have an important bearing on its subsequent experimental behaviour. In our experiments the leaves were severed under water and the cut ends were always supplied with water. They were then held in a saturated atmosphere and subjected to various periods of light and darkness. After this treatment they were immediately submerged in aerated, distilled water and strongly illuminated. Uptake of water by the cut ends was measured by means of a sensitive potometer.

In one experiment the leaves were stored in the dark for 15 hr. and absorption was not observed during a subsequent period of 9 hr. under conditions of complete submergence and strong illumination. Similarly, absorption was not observed when the above pre-treatment was followed by 12 hr. illumination and then by 3 hr. in the dark again.

Absorption did occur, however, when the leaves were stored for 15 hr. in the dark and then illuminated for a further 12 hr. The total uptake of one leaf during a period of 330 min. was 29·5 mm.^{3} and when the experiment was concluded absorption was still occurring at a rate of 2·4 mm.^{3} per hour. Under these conditions the magnitude of the force causing the water to enter is considerable. A single leaf raised a column of mercury to a height of 49 mm. during a period of 490 min.

Other experiments have been performed to determine the effect of varying the environmental factors during the actual observation period. Leaves cut at 5.0 p.m. and stored in the dark for 15 hr., did not absorb when submerged afterwards in aerated, distilled water and strongly illuminated, but did so when the carbon dioxide concentration of the water was raised. Bubbles of gas were rapidly evolved from the leaf, and starch accumulated.

Leaves pre-treated in the dark for 15 hr. also absorbed when submerged in aerated, distilled water in the dark, but the flow was invariably reversed after about 20 min. During this time the intercellular spaces of about one-third of the leaf area became injected with water. Complete injection occurred after a maximum period of 12 hr. submersion. Injection of the spaces has never been observed in submerged, illuminated leaves.

The absorption of water by the cut ends of submerged, illuminated leaves can therefore be related to the pre-treatment in the first instance. After cutting, illumination in a saturated atmosphere after a period of darkness will cause absorption to occur when the leaf is afterwards submerged and strongly illuminated. The effect of the light pre-treatment on the water uptake disappears if followed by a 3-hr. period in the dark. Absorption does not occur under the same conditions if the pre-treatment is carried out in a dark, saturated atmosphere, but does occur if the carbon dioxide concentration of the water is raised. Under these latter conditions rapid photosynthesis occurs.

It is possible that these findings may explain in part the divergent results of the earlier workers. Further experiments are now in progress to try to elucidate the mechanism causing the absorption.

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[1] Dixon, H. H., *Sci. Proc. Roy. Dublin Soc.*, **22**, No. 5, 55 (1938).
[2] Dixon, H. H., and Barlee, J. S., *Sci. Proc. Roy. Dublin Soc.*, **22**, No. 20, 211 (1940).
[3] Paauw, van der F., *Rec. Trav. Bot. Neerl.*, **32**. 202 (1935).
[4] Paauw, van der F., *Nature*, **166**, 231 (1950).
[5] Smith, F., Dustman, R. B., and Shull, C. A., *Bot. Gaz.*, **91**, 395 (1931).

Responses of *Cerianthus* to Stimulation

The neuromuscular activities of the Anthozoa have been studied extensively as examples of the working of the 'elementary nervous system'[1,2]. Most of the information in this field comes from the sea anemones, the order Actinaria, sessile animals which exhibit basic patterns of slow periodic activity together with certain quick protective responses. The latter are facilitated responses in which single electrical stimuli are ineffective; responses occur only to the second and subsequent stimuli of a series within a limited frequency-range[3].

Such studies influence our ideas about the evolution of the nervous system, and it is important, therefore, to extend them to as many groups of the Anthozoa as possible. In this connexion, the Ceriantharia are an obvious choice for investigation. They are a small and isolated order of tube-living anthozoans, found in North Atlantic and Mediterranean coastal waters. The musculature of the cerianthids differs greatly from that of other Anthozoa. It consists in the main of a thick and compact core of longitudinal muscle lying between the ectoderm and the mesoglœa. The contractions of this muscle pull the animal back into its tube by a series of sharp jerks whenever it is disturbed unduly by external stimuli.

This communication describes the results of some stimulation experiments on the species of *Cerianthus* found at Naples, *C. membranaceus* and *C. viridis*[4].

In my experience individual *Cerianthus* do not readily give closing responses to tactile stimuli. It is possible to handle the animal, even to pick it up in its tube, flick its tentacles or prod it sharply with a glass rod, without eliciting the powerful withdrawal movement. In this respect, *Cerianthus* differs markedly from anemones like *Calliactis* and *Metridium* which close down in response to quite gentle tactile stimulation. Since the latter do not respond to single electrical stimuli, it was surprising, therefore, to discover that the relatively insensitive *Cerianthus* always responds to any single supra-threshold stimulus, and shows no sign of facilitation in the response to a series of stimuli. Moreover, with the electrodes placed anywhere on the surface of the animal, even at the very tip of a single tentacle, one gets this powerful but apparently invariable withdrawal movement to the first and all subsequent stimuli at frequencies down to 0·25 sec.

Fig. 1*a* shows the response to a single stimulus (condenser discharge) with the electrodes brought up to the tip of a single tentacle. Fig. 1*b* shows the response to five stimuli at a frequency of 0·85 sec. with the electrodes near the base. The tracings, taken with a spring lever, show a uniform rise in tension with each stimulus, and at the end of this series the shortening of the animal was virtually complete. It is noteworthy that the tension was maintained for some time after the contraction and up to 1 min. almost no relaxation took place. The response follows the stimulus with a latent period of 0·05–0·10 sec. in different animals, and no marked differences in latency were detected when the electrodes were applied to various places on the surface of the animal.

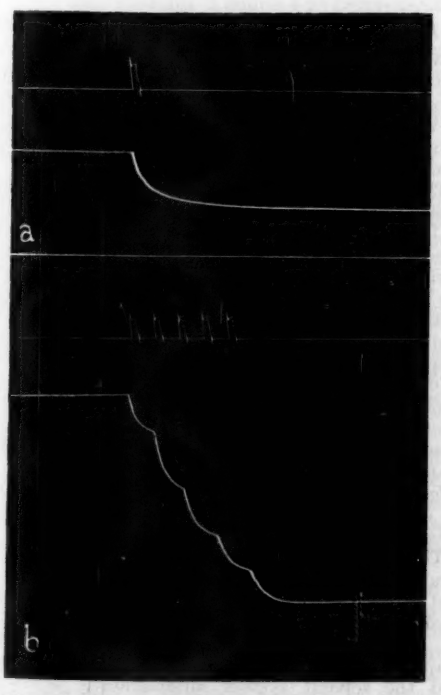

Fig. 1. *a*, Response of *Cerianthus* to a single electrical stimulus applied to the tip of a single tentacle; *b*, response of *Cerianthus* to five electrical stimuli at a frequency of 0·85 sec. applied to the aboral end

Both in responses to stimulation and in general behaviour, *Cerianthus* seems to be extraordinarily limited in its activities. No definite slow movements were recorded in animals attached to levers for several hours, and no slow movements were ever seen as distinguishable components in the responses to electrical stimuli. Yet the animal is certainly sensitive to light and to various chemical and food stimuli, but the nature of the response to such stimuli remains to be analysed.

These observations have a bearing on certain functional and phylogenetic problems. The neuromuscular equipment of *Cerianthus* is clearly a rapidly conducting, open-junction system. It resembles a giant-fibre/striped-muscle situation more than the nerve-net/slow-muscle system generally regarded as typical of the Anthozoa. Yet the all-or-none response of *Cerianthus* to single stimuli would be most unsuited to animals like *Calliactis* and *Metridium*, the neurosensory apparatus of which seems to be so much more easily excited. For these animals, facilitation acts as a safeguard against unnecessary closure; perhaps it should be regarded as an adaptation to that situation.

These results with *Cerianthus* make it clear that, even in the Anthozoa, the 'elementary nervous system' has to supply a complete range of effector types, from slow to fast, from rhythmically active to quiescent, and it must therefore display a corresponding range of nervous adaptations. The real value of the Anthozoa for studies in comparative neurophysiology is not that they are primitive in the phylogenetic sense, but that being mostly non-locomotory, their simple activities may be analysed with a fair measure of completeness[3].

I wish to thank the Director and Staff of the Stazione Zoologica, Naples, for their help and hospitality during my stay there, and the Council of the Royal Society for a grant from the Browne Fund, which made my visit possible.

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[1] Parker, G. H., "The Elementary Nervous System" (J. B. Lippincott, Philadelphia, 1919).
[2] Pantin, C. F. A., *Proc. Roy. Soc.* B, **140**, 147 (1952).
[3] Pantin, C. F. A., *J. Exp. Biol.*, **12**, 119 (1935).
[4] Torelli, B., *Pubbl. Staz. Zool. Napoli*, **12**, 1 (1932).

Cerianthus responds to a single condenser shock by a rapid contraction of tentacles and column. The response is symmetrical no matter where the shock is applied, from aboral end to tentacle tips, is propagated with a velocity of 1–2 m.sec., and is independent of the strength of the stimulus above threshold. The response is followed by an absolute refractory period of 60–70 m.sec. at 22–23° C. and a relative refractory period up to 200 m.sec. after the stimulus. For stimulation of either tentacles or column a threshold at twice the rheobase was obtained by discharge of a 0·05 μF. condenser through a total electrode-plus-preparation resistance of 3,000 ohms, thus giving a capacitance-resistance value of 0·15 m.sec. and

chronaxie of 0·05 m.sec. Non-polarizable zinc-sulphate–zinc-agar glass tube electrodes of 0·5 mm. orifice diameter were used. With the same apparatus the chronaxie of the column through-conducting system of Naples specimens of *Calliactis* was 1·0 m.sec. Hill's[1] equation for the excitation of nerve fits the strength-duration curve for *Calliactis* but does not approximate closely to that for *Cerianthus*. Complete curves of the strength-duration relation and the relative refractory period will be published elsewhere.

For a maximally facilitated contraction, the optimum interval between two effective shocks is 90–100 m.sec., and no facilitation is detectable with intervals greater than 1 sec. Except for the much shorter chronaxie, the excitable properties of the *Cerianthus* through-conducting system are therefore similar to those of the mesenteric system of *Calliactis*[2], but in *Cerianthus* there is as yet no evidence of co-ordination by nerves. The physiological observations indicate a nerve net of large fibres with rapid conduction and short chronaxie, but the histological picture does not fulfil these expectations. Ganglion cells and a nerve net of the usual type are reported to be absent in the expected positions[3]. In these circumstances the facilitation of contraction cannot be assumed to be neuromuscular. The relevant muscle fibres of tentacles and column are ectodermal.

A characteristic feature of *Cerianthus* is explained by the short chronaxie. The animal is remarkably tolerant to mechanical stimulation and rough handling. Histological studies show a great density of superficial primary sense cells, an anatomical picture which looks as if it would be very sensitive. The short chronaxie of the through-conducting system means that local excitation of it, such as electrotonic changes, decays very rapidly. Therefore the input from the sense cells to the through-conducting system is a differentiating filter with a short time-constant and high signal-to-noise ratio. It could allow only excitation of high frequency or from many sense cells in synchrony to pass. This is a crucial point for the natural excitation of the through-conducting system, which is thereby isolated from insignificant stimulation.

In addition to the rapid symmetrical response of the through-conducting system there is another set of co-ordinated slower responses of tentacles, disk and column which may be elicited by light, gravity, mechanical, chemical or sub-threshold electrical stimulation without causing an accompanying quick contraction. Electrical stimulation may arouse the faster and slower contractions simultaneously. A mechanically stimulated tentacle contracts and bends towards the mouth, and following stronger mechanical stimulation the neighbouring tentacles bend towards the mouth while the edge of the disk is raised. A slow bending of the column is produced by touch, by a series of sub-threshold shocks or by illumination. The time-scale of these slower responses is such that contractions may take 5 min., and relaxations are usually complete in 15–30 min. An animal resting in a glass tube makes continual local movements, particularly of the column end. A strip of column muscle left on the kymograph shows irregular slow movements for many hours, probably in part stimulated by the fixing pins. Following a quick twitch, a slower contraction may appear as a delay of the relaxation, which can then occupy 15–30 min., whereas a normal quick twitch has relaxed after 2 min. under a load of about 10 gm. The slower components of contractions are propagated along the muscle strip but less readily around the column. Two longitudinal strips, connected by a transverse bridge, give similar quick twitches but only the stimulated strip also gives the slower component.

The quick response to a single shock is clearly co-ordinated by a single all-or-nothing impulse which spreads over the whole ectoderm. Therefore any series of such impulses must be followed by a quick contraction. Therefore excitation which co-ordinates other activities cannot be transmitted by impulses in the same pathway. Previous histological work[3] and new methylene blue preparations as yet show the existence of only primary sensory cells, but no cell bodies or fibres of co-ordination neurones. A plexus of very thin fibres within the ectodermal layer has been described, but Torelli[3] does not consider these to be nervous elements.

If this histological picture be accepted, *Cerianthus* must have the simplest metazoan large-scale contraction mechanism, with two types of transmission and the muscle as the only component. But a preferable conclusion is that the exact locations of the co-ordination pathways remain obscure. Physiological properties so far available are alone not sufficient to allow a decision as to the presence or absence of a nerve net.

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[1] Hill, A. V., *Proc. Roy. Soc.*, B, **119**, 305 (1936).
[2] Pantin, C. F. A., *J. Exp. Biol.*, **12**, 119 (1935).
[3] Torelli, B., *Pubbl. Stat. Zool. Nap.*, **23**, 141 (1952).

A Growth Inhibitor of *L. bulgaricus* 09

While assaying skim-milk powder samples for orotic acid using *L. bulgaricus* 09, by the method of Wright *et al.*[1], the presence of a substance inhibitory to the growth of this organism was detected in samples which had been stored at 60° C. for six months.

This inhibitor was also formed when skim-milk powder was heated at 100° C. for 5 hr. or autoclaved at 15 lb. pressure for 30 min. Further, autoclaving lactose with any of the proteins, casein, edestin, fibrin, hæmoglobin, or with tryptone or with any of the following amino-acids, leucine, *iso*leucine, valine, methionine and glycine, led to the formation of the inhibitor. Concentrates of the inhibitor have been prepared from samples of skim-milk powder stored at 60° C. for six months, by extraction with acetate buffer at *p*H 4·6, followed by extraction with ether and from autoclaved mixtures of casein and lactose by extraction with benzene. The growth-inhibitory activity of these preparations for *L. bulgaricus* 09 was determined, and they were found to cause complete inhibition of growth at levels between 200 and 400γ per ml. of medium.

This growth inhibitor was soluble in water and in a number of solvents such as ether, benzene, alcohol and butanol. It was adsorbed on charcoal at *p*H 4·6. Hydrolysis with acid or alkali was found to inactivate it. By employing the ascending-paper chromatographic technique, using Whatman No. 1 filter paper and the solvent system butanol/acetic acid/water (4 : 1 : 5), it was found that the inhibitor concentrate gave a spot (R_F = 0·89) which answered the benzidine test for reducing substances and the Rydon and

Smith test[2] for peptides but was negative to ninhydrin. However, when the inhibitor concentrate was hydrolysed with 2 *N* hydrochloric acid at 100° C. for 20 hr. and chromatographed similarly, 4–5 ninhydrin-positive spots were obtained, depending upon the source from which the inhibitor had been extracted.

These properties, together with the fact that the inhibitor is formed on autoclaving lactose with a number of proteins, tryptone and amino-acids, indicate that it is peptide in nature.

Further studies on the exact composition of this inhibitor and its mode of action are in progress and will be reported elsewhere.

We are indebted to Dr. L. D. Wright, Cornell University, for the culture of *L. bulgaricus* 09 and to the Madras State Research Committee for financial assistance during the course of this study.

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[1] Wright, L. D., Valentik, K. A., Spicer, D. S., Huff, J. W., and Skeggs, H. R., *Proc. Soc. Exp. Biol. Med.*, **75**, 293 (1950).
[2] Rydon, H. N., and Smith, P. G. W., *Nature*, **162**, 922 (1952).

Pigments and Pterins in the Skin of the Green Mamba, *Dendroaspis viridis*

It has previously been reported that the skins of the green snakes *Philothamnus semivariegatus* and *Dispholidus typus* contain riboflavin, *iso*xanthopterin and 2-amino-4-hydroxpteridine-6-carboxylic acid[1,2]. *D. typus* also contains 2-amino-4-hydroxypteridine[2] and an unknown yellow pigment[1].

After this investigation had been completed, a single male specimen of the green mamba, *Dendroaspis viridis*, became available to us. The anterior and middle portions were leaf green, and the posterior portion dull yellow.

The animal was skinned and the skin cut into the green and yellow portions.

The yellow skin was extracted with 50 ml. portions of boiling 80 per cent aqueous ethanol, in the dark, until the extract was colourless. The combined extracts were evaporated to dryness, the residue dissolved in 50 ml. of *N*/4 aqueous ammonia and the solution filtered from insoluble material. Analysis of this solution by paper chromatography showed the presence of a yellow non-fluorescent pigment; and, on viewing in 365 mμ light, an additional yellow fluorescent substance, a purple fluorescent substance, a bright blue fluorescent substance and a blue fluorescent substance.

The yellow fluorescent substance was identified as riboflavin by its similar behaviour to an authentic sample in three solvent systems; pyridine/propanol/water (3 : 1 : 1 by vol.); tert-butanol/pyridine/water (50 : 15 : 35 by vol.); and tert-butanol/pyridine/water (60 : 15 : 25 by vol.).

The purple fluorescent substance was identified as *iso*xanthopterin, the bright blue fluorescent substance as 2-amino-4-hydroxypteridine-6-carboxylic acid, and the blue fluorescent substance as 2-amino-4-hydroxpteridine. This was done by comparing their behaviour with that of authentic samples in the three previous solvent systems and in butanol/acetic acid/water (4 : 1 : 5 by vol.); 5 per cent aqueous acetic acid (by vol.); and 3 per cent aqueous ammonium chloride.

The yellow non-fluorescent substance could not be identified. Its chromatographic behaviour in butanol/acetic acid/water (4 : 1 : 5 by vol.) was similar to that of the unknown yellow pigment in *D. typus*[1].

The green portion of the skin was extracted with 50 ml. portions of boiling 80 per cent aqueous ethanol until the extract was colourless. The extracts were combined, and the presence of riboflavin and *iso*xanthopterin was shown by paper chromatography, as before. No attempt was made to identify 2-amino-4-hydroxypteridine-6-carboxylic acid nor 2-amino-4-hydroxypteridine in the ethanolic extract. The yellow non-fluorescent substance was present.

I am grateful to Mr. A. H. Booth of the Zoology Department of this College for supplying the specimen of *D. viridis*; and to the Chemical Society for a grant in aid of this investigation.

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[1] Blair, J. A., and Graham, J., *Biochem. J.*, **56**, 286 (1954).
[2] Blair, J. A., and Graham, J., *Chem. and Ind.*, 1158 (1955).

Onset and Cessation of Hibernation under Constant Temperature and Light in the Golden-mantled Ground Squirrel (*Citellus lateralis*)

Towards the end of the summer of 1955 we received, through the kindness of Dr. J. E. Moore (University of Alberta), a number of golden mantled ground squirrels (*Citellus lateralis*). These animals had been trapped during August–September in the Turner Valley, Alberta, and were shipped to Toronto by express. Our stock was further replenished in the same manner during the summer of 1956.

One of the experiments we have undertaken involved placing a squirrel in a cold room with a mean temperature of about 35° F. (min., 30° F.; max., 42° F.) and leaving it there indefinitely. At the present time (July 1957) one animal has been there for nearly two years, and during this time has had ample bedding, food and water *ad lib.*, and has been subject to an artificial 12-hr. day throughout. Or to put it another way, the animal has been removed from all known seasonal fluctuations in temperature, light and availability of food. Notwithstanding this, it seems remarkable that the squirrel has hibernated only at 'the right time of year', that is, autumn–winter (October–May) and has been active only at the 'right time of year', that is, spring–summer (June–September).

Thus far only one animal has been under these constant conditions for this length of time. However, from data on eight other animals (3 males, 5 females) which have been in our possession for the same length of time, but which have been subject to varying conditions of temperature, light, food and access to exercise wheels, all show a tendency to hibernate over the winter months and to be active in the summer months regardless of the temperature and the length of the artificial day. During June–September denial of food, which is accompanied by a large drop in weight, will after several days force the animal to hibernate; but it cannot survive this for long, whereas

during the normal winter hibernating period, practically no food is consumed for seven or eight months.

Of thirteen additional animals which have been in our possession now for ten months, nine (4 males, 5 females) have been kept in constant cold from October 1, 1956, to the present (July 1957), and all but one of these hibernated over the winter months, and again with the exception of one, all became active in the spring. It should be noted here that a gradually decreasing length of the artificial day in the autumn, down to 7 hr., did not induce hibernation earlier than those in a constant 12-hr. day. Furthermore, in March, prior to the animals becoming active, the length of the day in three cases was reduced to 4 hr. and in two cases increased to 20 hr., but even this caused no significant difference in the time at which the animals became active and continued in that state. It seems, however, that access to an exercise wheel in the autumn tends to delay the onset of hibernation for about a month, but once the animal enters hibernation it continues in this state until approximately the same time as those which are denied an exercise wheel.

It is still conceivable that the organisms we have studied have received clues concerning the seasons from some other variations such as noise level, from barometric pressure changes or from variations of the water content of the air. None of these factors seems likely to us to be of appreciable significance however. Instead, it seems necessary to conclude that the species in question possesses some form of 'internal seasonal clock' which determines the periods of hibernation and activity, and which is independent of the normal seasonal fluctuations of temperature and light, and is not governed by the food supply.

The Columbian ground squirrel (*Citellus columbianus*) and the thirteen-lined ground squirrel (*Citellus tridecemlineatus*) also seem to show the same type of phenomenon, though our results from these animals is as yet rather scanty.

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Susceptibility of the Hedgehog (*Erinaceus europaeus*) to Infection with *Leptospira pomona*

Leptospira pomona is widely distributed in New Zealand, and outbreaks of leptospirosis among farm animals cause considerable economic loss to the livestock industry. While it is generally accepted that the domestic pig is the normal reservoir of infection it is rarely possible to inculpate the pig directly in ovine outbreaks of leptospirosis, and many outbreaks also occur on dairy farms on which no pigs are kept.

In view of its feeding habits, the hedgehog, which was introduced into New Zealand some sixty years ago and has now become extremely numerous in most districts, suggested itself as a possible alternative reservoir of infection.

I have recently caught some thirty hedgehogs in a suburban garden area and inoculated them with a culture of *L. pomona* which has been maintained in this laboratory since its isolation from an ovine outbreak of the disease in 1953. Every hedgehog contracted a clinical leptospirosis, and the disease appears to run a remarkably characteristic course in this species.

Small young and half grown individuals almost invariably die with some or all of the signs of classical Weil's disease (l. icterohaemorrhagiae), that is, recurrent febrile peaks with sub-normal intermissions, icterus, meningitis, 'butterfly' lungs, and typical degenerative lesions in spleen, liver and kidneys. Those surviving long enough commence urinary excretion of the organisms around the 16th–18th day.

Adults usually survive the challenge infection but excrete the organisms in their urine over a period and develop high agglutination-lysis titres to *L. pomona* antigen. Pregnant females may abort.

Guinea pigs inoculated with emulsified liver and kidney substance obtained from infected hedgehogs at post mortem and also with the stomach content of aborted fœtuses gave a typical response and the organisms were recovered from them.

By the time these experiments were completed winter had set in and most hedgehogs were in hibernation; but I have just examined two individuals found after a careful search on a dairy farm on which a severe outbreak of leptospirosis had recently occurred. Both these adult hedgehogs revealed typical leptospiral lesions on post-mortem examination; the organisms were present in the urine of one, and the blood serum of both had agglutination-lysis titres in excess of 1/3,000 against *L. pomona* antigen.

The hedgehog has thus proved highly susceptible to experimental infection with the strain of *L. pomona* used here and it has also been established that natural infection may occur in the field. As soon as these animals become active again in the coming spring it is intended to carry out a survey to determine the extent of natural infection.

Hitherto the hedgehog has only found a very limited use as a laboratory animal in virology research, but in the light of the results here reported it may prove a useful tool in leptospiral research in general.

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The Sheep Lungworm *Protostrongylus brevispiculum* in Great Britain

During the past year observations have been made to assess the seasonal pattern of lungworm infection in a flock of sheep grazing on the Wiltshire Downs. In the course of the examination of fæcal samples from some of these animals first stage lungworm larvæ of an unusual type were encountered. A description of such larvæ could not be found in the literature. A search for the adults was, therefore, made. This proved to be more complex than had been anticipated as a number of lungworm species new to us were found. One of these has been identified as *Protostrongylus brevispiculum*, and the present record is thought to be the first of the occurrence of this lungworm in sheep in Great Britain.

The only records and descriptions of this lungworm are those of Mikaðiè[1], who found specimens in sheep

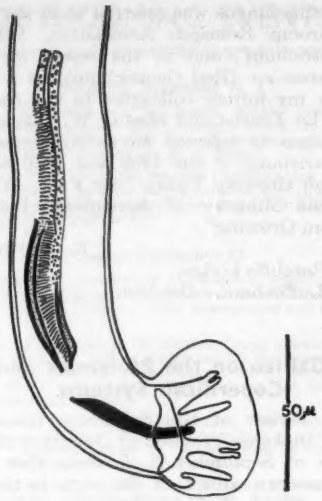

Fig. 1. Lateral view of hind end of male *Protostrongylus brevispiculum*

in Yugoslavia. He named the worm *Protostrongylus rupicaprae* (Gebauer, 1932) *brevispiculum*; this is amended to *P. brevispiculum* by Dougherty and Goble[2] in their classification of the subfamily Protostrongylinae.

Mikačić's original descriptions are somewhat incomplete, being based mainly on a detailed study of the hind end of the male worm, and it is mainly from this description that our specimens have been identified as *P. brevispiculum*.

The worms are similar in general appearance to *Muellerius capillaris*, being small and hair-like. An intact male measured 5 mm. long by 0·033 mm. wide. The bursa of the male is, however, of the typical protostrongylin type (Fig. 1). The dorsal ray is small and rounded, the externo-dorsals are elongate. The postero- and medio-laterals are fused along most of their length, while the antero-laterals are separated from them. The ventro and latero-ventral rays are united along the greater part of their length, forming a very distinctive conical base. The spicules, between 110–130μ long, the crura of the gubernaculum 30–33μ long, and the telemon are all clearly visible.

This worm is found within the lung tissues in lesions which on superficial examination are identical with those resulting from infection with *M. capillaris*. In most of the lungs examined both species of lungworm were frequently recovered from one and the same lesion. Although only a limited number of lungs have been examined and as yet there are insufficient data to assess the incidence of this lungworm in the flock, the indications are that it is by no means rare.

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[1] Mikačić, D., *Vet. Arhiv.*, **9**, 126 (1939); **10**, 86 (1940).
[2] Dougherty, E. C., and Goble, F. C., *J. Parasit.*, **32**, 7 (1946).

Detection of the Substrate of Enzymic Browning in Cacao by a Post-chromatographic Enzymatic Technique

The polyphenols of the cacao bean have been described by Forsyth[1], who has demonstrated the presence of four catechins, three leucocyanidins and two anthocyanins. It is evident from his observations and my own (unpublished) that other phenolic materials remain to be identified.

In view of the importance of enzymic browning in the commercial drying of cacao, experiments have been undertaken to determine the relative importance of the polyphenols of the bean in the browning process. To this end, a post-chromatographic enzymatic technique was developed which was designed not only to assess the contribution of each of the known polyphenols to the browning process but also to detect the presence of any hitherto undetected phenolic compounds, which might give rise to browning under the influence of polyphenol oxidase.

Freshly harvested cacao beans were macerated in methanol in a Waring blendor for three minutes. The suspension was then filtered and the residue exhaustively washed with methanol until the washings were colourless and no longer reacted with a 1 per cent solution of ferric chloride. The residue was white in colour, and although it exhibited a high polyphenol oxidase activity in aqueous solution on the addition of substrate no browning of the aqueous suspension occurred in the absence of added substrate. It was therefore concluded that all of the naturally occurring substrate of enzymic browning was removed from the residue of the bean by exhaustive methanolic washing. That a non-browning leucocyanidin material was however present in the residue was shown by the production of cyanidin on digestion of the residue with 2 *N* aqueous hydrochloric acid[2].

Methanolic extracts of both Forastero and Criollo type beans were then applied to a chromatogram, which was formed into a cylinder and developed with butanol–acetic acid–water (40 : 10 : 50) for 16 hr. The chromatogram was then dried at room temperature and heavily sprayed with a filtered aqueous solution of the methanol-washed residue which had been shown to possess a high polyphenol oxidase activity. The chromatogram, still in cylindrical form, was then placed on a wire gauze platform over a shallow layer of water contained in a glass tank. The lid was sealed into position with lanolin and the tank incubated at 40° C. By means of this apparatus, it is possible to maintain the chromatogram in a moist and highly aerobic condition in a humid atmosphere and at the optimum temperature of the phenoloxidase for an indefinite period. Under these conditions the oxidative enzymic reactions go to completion and brown colorations develop on the chromatograms in the position of the original phenolic substrates. By comparison of such chromatograms with similar chromatograms sprayed with phenolic reagents, namely, ferric chloride/potassium ferricyanide[3] or diazotized *p*-nitro-aniline[3], the identification of the major polyphenols concerned in enzymic browning may be effected.

Examination of the enzymatically treated chromatograms of extracts of Forastero and Criollo type beans indicated that in both cases the major substrate of enzymic browning was (−)-epi-catechin, a large and intense region of browning being found in a

position corresponding to an R_F of 0·65. The formation of brown pigmentation occurred only in traces elsewhere on these chromatograms, although the presence of large amounts of phenolic material of low R_F value was detected by the diazotized *p*-nitro-aniline reagent on the control chromatograms. Similar results were obtained when a 1 per cent aqueous hydrochloric acid extract of the beans was examined by this technique.

In a further series of experiments, in which two-dimensional chromatograms, developed first with water and secondly with butanol–acetic acid–water, were submitted to the enzymatic treatment, although essentially the same phenomena were observed, the greater degree of resolution of the polyphenols revealed slight browning in the position of the faster moving leucocyanidin (L_1 leucocyanidin of Forsyth, 1955). Prolonged incubation did not result in any increase in the intensity of the spot, which remained weak. These observations indicate that the leucocyanidins are not an important substrate of browning in the cacao bean.

The two anthocyanins, which appeared on the untreated chromatograms as purple spots of R_F 0·33 and 0·41, were observed on incubation of the enzymatically treated chromatograms to become slowly colourless and afterwards to give rise to faint brown colorations.

Since it appeared possible that further phenolic material might be rendered susceptible to polyphenol oxidase action in the course of the commercial fermentation process, to which the beans are subjected prior to drying, methanolic extracts of fermented beans were prepared and examined by the above technique. No additional substrates were, however, detected in fermented material and the only difference noted was a reduction in the amount of brown pigmentation in the epi-catechin position. This was however expected as Forsyth[1] has reported a loss of epi-catechin by exudation from the bean during fermentation.

It would thus appear that in the cacao bean (−)-epi-catechin is the major substrate of polyphenol oxidase and accordingly that the (−)-epi-catechin content of the cacao bean at the end of fermentation is a major factor in the subsequent enzymic browning of the bean. It is, moreover, evident that the leucocyanidins, which are present in the cacao bean in quantities comparable to those of the catechins (Forsyth, 1955), contribute to a very limited extent to the enzymic browning of the bean.

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[1] Forsyth, W. G. C., *Biochem. J.*, **51**, 511 (1952); **60**, 108 (1955).
[2] Bate-Smith, E. C., *Chem. and Ind.*, 1457 (1954).
[3] Barton, G. M., Evans, R. S., and Gardner, J. A. F., *Nature*, **170**, 249 (1952).

Sporendonema

My attention has been directed to a letter published in *Nature* of February 9, 1957, by F. C. Wood on *Sporendonema*, in which it is stated that the fungus known to mushroom growers as 'red *Geotrichum*' and 'lipstick mould' is invariably referred to as *Geotrichum* sp. The letter proceeds to report its identification by Mason and Hughes as *Sporendonema purpurascens*.

In fact this fungus was referred to in the report of the Mushroom Research Association, 1946–48, as 'Red Geotrichum', and in the report for 1949 as *Sporendonema* sp. (Red Geotrichum), as a result of studies by my former colleagues in the Association, Dr. C. J. La Touche and Miss C. W. Duncan.

The fungus is referred to as *Sporendonema* sp. (Red Geotrichum) in the 1950 and 1956 editions of "Mushroom Growing Today", by F. C. Atkins, and also in the Ministry of Agriculture Bulletin 34, "Mushroom Growing".

R. L. Edwards

Ratcliffe Lodge,
South Luffenham, Oakham.

Galileo on the Ptolemaic and Copernican Systems

In my review of the Salusbury translation of Galileo's "Dialogue", revised by Giorgio de Santillana, in *Nature* of September 7, I wrote that this was the first modern edition of the work in the English language. Mr. J. B. Mack, librarian of Lehigh University, Bethlehem, Pennsylvania, has, however, directed my attention to an earlier English translation, which was published in 1953[1]. I hasten to repair the injustice involuntarily done to the author of the latter work.

Having been struck some two decades ago by the strange fact that a work ranking so high among the classics of science was not available in English, Mr. Stillman Drake, of Puerto Rico, undertook the task of repairing this breach in the literature of the history of science and fulfilled it after ten years strenuous labour, during which time he became a possibly unparalleled connoisseur of Galileo's life and work in general. He made his translation from the original text as published in Vol. 7 of the Edizione Nazionale, and, as a comparison will readily show, bestowed the utmost care on it.

This does not mean that he felt obliged to give a strictly literal rendering of the text. He rightly believed that the translation should make as easy and fascinating reading to a non-specialist of our times as the original must have made for cultivated and interested Italians of the seventeenth century. In this, I believe, he succeeded remarkably well. His work will certainly contribute in making a most important and influential classic accessible to the modern reader.

The value of the translation is enhanced by giving (between square brackets) the additions which Galileo made to the work after the first edition of 1632. It is a good thing also that his marginal notes, which often are omitted in modern editions, have been retained.

Only one critical remark should be made. The title of the "Dialogue" is reproduced in this translation in a convenient but highly abbreviated form. No objection can be made to this, but one regrets that the exact and complete rendering of its wording is nowhere to be found.

E. J. Dijksterhuis

Wagnerlaan 27, Bilthoven,
The Netherlands.

[1] "Galileo Galilei, Dialogue Concerning the Two Chief World Systems —Ptolemaic and Copernican". Translated by Stillman Drake. Foreword by Albert Einstein. Pp. xxvii+496. (University of California Press, Berkeley and Los Angeles, 1953.)

FORTHCOMING EVENTS

*(Meeting marked with an asterisk * is open to the public)*

Monday, December 16

INSTITUTION OF ELECTRICAL ENGINEERS, RADIO AND TELECOMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Informal evening on "Electronics and Automation—Electronics in the Textile Industry". Talk by Mr. K. J. Butler.

BRITISH COMPUTER SOCIETY (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Dr. S. Gill: "Parallel Programming—a Study of a New Technique in Digital Computer Programming".

Tuesday, December 17

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Mr. J. S. Cramer: "The Depreciation and Mortality of Motor Cars".

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the INSTITUTIONS OF CIVIL and of MECHANICAL ENGINEERS, at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Sir Ewart Smith: "The Engineer and Management" (Fourth Graham Clark Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. J. Lamb: Informal lecture on "Recent Uses of Ultrasonics in Investigating the Characteristics of Materials".

PLASTICS INSTITUTE, LONDON AND DISTRICT SECTION (at the Wellcome Building, 183–193 Euston Road, London, N.W.1), at 6.30 p.m.—Mr. C. W. Welch: "The Plastics Institute, Press and Industry" (Chairman's Lecture).

Wednesday, December 18

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 2.30 p.m.—Discussion on "Teaching Corrosion Science". "Existing Facilities for Training in Corrosion Science" opened by Mr. L. W. Stubbs; "Future Requirements" opened by Dr. T. P. Hoar.

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, South Kensington, London, S.W.7), at 5 p.m.—Mr. J. L. Monteith: "Dew"; Mr. N. E. Rider: "Water Losses from Various Land Surfaces".

ROYAL STATISTICAL SOCIETY (at University College, Gower Street, London, W.C.1), at 5.15 p.m.—Prof. J. Neyman and Prof. Elizabeth Scott: "Statistical Approach to Cosmology".

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. E. Garthwaite, M.B.E., and Mr. A. G. Wray: "Recent Developments in Electronic Instrument Design".

SOCIETY FOR ANALYTICAL CHEMISTRY, BIOLOGICAL METHODS GROUP (at "The Feathers", Tudor Street, London, E.C.4), at 6.30 p.m.—Annual General Meeting, followed by a Joint Meeting with the MICROCHEMISTRY GROUP. Discussion on "The Weighing and Measurement of Small Quantities", opened by Dr. G. F. Hodsman and Mr. R. Goulden.

OIL AND COLOUR CHEMISTS' ASSOCIATION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Dr. L. A. O'Neill: "Polyvinyl Acetate Emulsion Paints: Solved and Unsolved Problems".

SOCIETY OF COSMETIC CHEMISTS OF GREAT BRITAIN (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7.30 p.m.—Dr. R. H. Marriott: "Penetration of Skin—Dead or Alive".

Thursday, December 19

INSTITUTION OF MINING AND METALLURGY (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—General Meeting.

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. N. Aaronszajn: "Finite Dimensional Perturbation and Spectral Problems".

INSTITUTE OF FUEL (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Dr. W. Idris Jones, C.B.E.: "Russian Coal Mining and Fuel Technology".*

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. D. C. Soul and Mr. R. E. Davidson: "The Whiting–Oil Relationship in Glazing Putty"; Dr. J. Bowler-Reed: "The Examination of Building Mastics and Similar Compositions".

Thursday, December 19—Friday, December 20

PHYSICAL SOCIETY (at Imperial College, London, S.W.7)—Conference on "The Band Theory of Metals and Experimental Investigations into the Structure of the Fermi Surface".

Friday, December 20

INSTITUTE OF NAVIGATION (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—Rear-Admiral K. St. B. Collins, O.B.E., D.S.C.: "Admiral Francis Beaufort, His Contribution to Hydrography and Navigation".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER IN BACTERIOLOGY—The Secretary, North of Scotland College of Agriculture, 41½ Union Street, Aberdeen (December 20).

RESEARCH SCHOLAR (honours graduate in chemistry or physics) IN THE PHYSICOCHEMICAL LABORATORIES, to carry out research work on the flow properties of polymers and coal—The Registrar, The Manchester College of Science and Technology, Manchester 1 (December 20).

SENIOR LECTURER (with a degree in psychology, preferably with biology, mathematics or physics) IN PSYCHOLOGY in the Department of Management and Production Engineering—The Principal, Brunel College of Technology, Woodlands Avenue, London, W.3 (December 21).

ASSISTANT IN ENTOMOLOGY in the Department of Zoology—The Secretary, The University, Edinburgh (December 28).

BOTANICAL ASSISTANT, for duties which include teaching elementary botany and the identification and labelling of plants—The Director, The Royal Horticultural Society's Gardens, Wisley, Ripley, Surrey (December 28).

DEMONSTRATORS (2) (male graduates) in each of the following subjects: PHYSICS, CHEMISTRY, CIVIL OR MECHANICAL ENGINEERING, at the Royal Military College of Science, Shrivenham, Berkshire—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.30/7A (December 30).

LECTURER (preferably with a knowledge of nuclear engineering, heat transfer or mechanical design) IN ENGINEERING (MECHANICAL)—The Registrar, The University, Manchester (December 31).

SENIOR LECTURER IN APPLIED MATHEMATICS at the University College of Ghana—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 3).

BIOMETRICIAN in the Ministry of Agriculture, Federation of Rhodesia and Nyasaland, for duties which include the design of experiments in all phases of agriculture and animal husbandry research and analysis of data and related statistical practice—The Secretary (E), Rhodesia House, 429 Strand, London, W.C.2 (January 4).

CHAIR OF ENGINEERING STRUCTURES tenable at the Imperial College of Science and Technology—The Academic Registrar, University of London, Senate House, London, W.C.1 (January 6).

READER IN EXTRACTION METALLURGY at the Imperial College of Science and Technology—The Academic Registrar, University of London, Senate House, London, W.C.1 (January 13).

STATISTICIAN, Scientific Officer or Senior Scientific Officer grade (with a good honours degree and preferably postgraduate experience)—The Secretary, East Malling Research Station, near Maidstone, Kent (January 17).

LECTURER IN ELECTRICAL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (January 18).

CHAIR OF ZOOLOGY tenable at Queen Elizabeth College—The Academic Registrar, University of London, Senate House, London, W.C.1 (January 21).

SENIOR LECTURER OR LECTURER IN ZOOLOGY at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, January 30).

ASSISTANT LECTURER (man or woman graduate) IN MATHEMATICS, preferably APPLIED—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (January 31).

CHAIR OF BOTANY—The Registrar, University College of Wales, Aberystwyth (January 31).

CURATOR (with a university degree in one of the natural history subjects, or an equivalent qualification, and experience in museum administration, and preferably with the Diploma of the Museums Association) OF THE HANCOCK MUSEUM—The Hon. Secretaries, Natural History Society of Northumberland, Durham and Newcastle-upon-Tyne, The Hancock Museum, Newcastle-upon-Tyne 2 (January 31).

LECTURER IN PHYSICS at the University of Cape Town, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Cape Town, January 31).

LECTURER or ASSISTANT LECTURER IN MATHEMATICS at Makerere College, University College of East Africa—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 31).

LECTURER or ASSISTANT LECTURER IN PHYSICS at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (February 15).

PROFESSOR (with a university degree in science or in agriculture, and special qualifications and experience in teaching or research) OF PLANT SCIENCE (AGRICULTURAL BOTANY) at Canterbury Agricultural College (University of New Zealand)—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, February 15).

READERS (2) IN MATHEMATICS, one in the field of pure mathematics and the other in the field of applied mathematics, at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, February 28).

SENIOR LECTURER IN PURE or APPLIED MATHEMATICS at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, February 28).

DIRECTOR OF THE INSTITUTE OF BIOLOGICAL CONTROL, Ottawa, Canada; ASSISTANT DIRECTOR OF THE INSTITUTE OF ENTOMOLOGY, London; and ASSISTANT DIRECTOR OF THE BUREAU OF DAIRY SCIENCE AND TECHNOLOGY, Shinfield, near Reading, Berks—The Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, Bucks (March 31).

ANALYSTS, Experimental Officer grade (not under 26 years of age, with at least G.C.E. in five subjects including English language

(Ordinary) and chemistry and one other scientific or mathematical subject (Advanced) or equivalent qualifications), for the examination of radioactive materials—The Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berkshire, quoting Ref. 1641/34.

ASSISTANT (preferably with electronics experience) to help in biophysical research—The Medical Research Council, Biophysics Research Unit, King's College, Strand, London, W.C.2.

BIOCHEMIST, Senior or Basic grade (with a B.Sc. degree with honours in chemistry or biochemistry, or equivalent qualification)—The Group Secretary, Royal Hospital, Wolverhampton.

CHEMIST (aged 23–26, with a good B.A. or B.Sc. honours degree, and interested in organic and physical chemistry), to join a small team carrying out fundamental research—The Assistant Secretary, Ref. D.47, The British Coal Utilization Research Association, Randalls Road, Leatherhead, Surrey.

CHEMISTS, Scientific Officer or Senior Scientific Officer grade (with a first- or second-class honours degree in chemistry or equivalent), at the Road Research Laboratory (D.S.I.R.), Harmondsworth, Middlesex, for research on the use and performance of bituminous road materials and on problems arising from the presence of organic matter in soils—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting F.647/7A.

LECTURER (with teaching and research experience, preferably in applied entomology or soil zoology) IN AGRICULTURAL ZOOLOGY—The Registrar, The University, Nottingham.

PHYSICIST (Basic grade), for work connected with the medical applications of radioactive isotopes and general dosimetry of X-radiation—The Group Secretary, Nottingham General Hospital, Nottingham.

PHYSIOLOGICAL RESEARCH ASSISTANT (university graduate, with experience of experimental methods and of neuro-physiology) IN THE OTOLOGICAL INVESTIGATION UNIT, for work which includes investigation of the physiological reaction of the two parts of the internal ear in the human subject and also experimental research in the physiology and neurophysiology of the acoustic and vesicular system—The Secretary, Institute of Laryngology and Otology (University of London), 330/332 Gray's Inn Road, London, W.C.1.

RESEARCH ASSISTANT (with a science degree) IN THE DEPARTMENT OF PHYSIOLOGY AND BIOCHEMISTRY—The Head of the Physiology and Biochemistry Department, The University, Southampton.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

National Union of Journalists. Freelance Directory, 1957. Pp. i+65. (London: National Union of Journalists, 1957.) [269

The Nuffield Foundation. Report for the year ended 31 March, 1957. Pp. 168. (London: The Nuffield Foundation, 1957.) [269

Department of Scientific and Industrial Research. Summary of Progress of the Geological Survey of Great Britain and the Museum of Practical Geology for the year 1956; with the Report of the Geological Survey Board and Report of the Director. Pp. iv+84. (London: H.M. Stationery Office, 1957.) 4s. 6d. net. [269

Bulletin of the British Museum (Natural History). Entomology. Vol. 5, No. 5: The Pseudococcidæ (Hom.: Coccidæ) from East Africa Described by H. C. James. By G. de Lotto. Pp. 183–232. 15s. Vol. 5, No. 6: A Revision of the Genus *Neozephyrus* Sibatani and Ito (Lepidoptera: Lycaenidae). By T. G. Howarth. Pp. 233–272. 15s. (London: British Museum (Natural History), 1957.) [269

The Scottish Society of the History of Medicine. Report of Proceedings, 1956–57. Pp. 18+2 plates. (Edinburgh: Scottish Society of the History of Medicine, 1957.) [269

British Scientific Instrument Research Association. Descriptive brochure. Pp. 36. (Chislehurst: British Scientific Instrument Research Association, 1957.) [269

University of Leeds. Publications and Titles of Theses, 1954–55. Pp. 73. (Leeds: The University, 1957.) 6d. [269

World Federation for Mental Health. Mental Health and the World Community: Twelve Papers arising from an International Symposium held in Toronto, August, 1954. Edited by Prof. F. Brockington. Pp. vi+118. 10s. net. Mental Health Aspects of Urbanization. (Report of a Panel Discussion conducted in the Economic and Social Council Chamber, United Nations, New York, March 11, 1957, by the World Federation for Mental Health.) Pp. 46. 6s. net. (London: World Federation for Mental Health, 1957.) [269

Some Problems of the Atomic Age. By Prof. C. A. Coulson. (Second Scott Lidgett Memorial Lecture.) Pp. 40. (London: The Epworth Press, 1957.) 3s. 6d. net. [269

Department of Scientific and Industrial Research. Fuel Research 1956: Report of the Fuel Research Board with the Report of the Director of Fuel Research for 1956. Pp. iv+80+4 plates. (London: H.M. Stationery Office, 1957.) 4s. 6d. net. [269

British Medical Bulletin, Vol. 13, No. 3 (September, 1957): Autonomic Nervous System. Pp. 153–230+ix. (London: British Council, 1957.) 20s. [269

Discovery Reports. Vol. 29, pp. 141–198+plates 8 and 9: Isopod Crustacea. Part 2: The Sub-order Valvifera. Families: Idoteidae Pseudidotheidae and Xenarcturidae Fam. N. With a Supplement to Isopod Crustacea, Part 1. The Family Serolidae. By Edith M. Sheppard. (Cambridge: At the University Press, 1957.) 27s. 6d. net. [269

Hydrography of the Faroe–Shetland Channel, 1927–1952. By Dr. John B. Tait. (Scottish Home Department. Marine Research, 1957, No. 2. Pp. ix+309. (Edinburgh and London: H.M. Stationery Office, 1957.) 105s. net. [309

Water Research Association. Second Annual Report, 1956–57. Pp. 35. (Redhill: Water Research Association, 1957.) [309

Other Countries

Northern Region of Nigeria. Annual Report on the Forest Administration of the Northern Region of Nigeria for the year 1955–56. Pp. ii+39. (Kaduna: Government Printer; London: Crown Agents for Overseas Governments and Administrations, 1957.) 9d. net. [269

United States Department of the Interior: Geological Survey. Water Supply Paper 1251: Quality of Surface Waters of the United States, 1952. Part 5–6: Hudson Bay and Upper Mississippi River Basins, and Missouri River Basin. Prepared under the direction of S. K. Love. Pp. x+478. 1.50 dollars. Water-Supply Paper 1254: Geology and Ground-Water Features of the Smith River Plain, Del Norte County, California. By William Back. Pp. iv+76+7 plates. n.p. Water-Supply Paper 1330–D: Water Requirements of the Rayon- and Acetate-Fibre Industry. By Orville D. Mussey. Pp. vi+141–180. 20 cents. Water-Supply Paper 1348: Surface Water Supply of the United States, 1954. Part 14: Pacific Slope Basins in Oregon and Lower Columbia River Basin. Prepared under the direction of J. V. B. Wells. Pp. ix+291. 1 dollar. Water-Supply Paper 1371: Ground-Water Resources of the Ainsworth Unit, Cherry and Brown Counties, Nebraska. By James G. Cronin and Thomas G. Newport. Pp. v+120+2 plates. n.p. Water-Supply Paper 1389: Surface Water Supply of the United States, 1955. Part 6-A: Missouri River Basin above Sioux City, Iowa. Prepared under the direction of J. V. B. Wells. Pp. x+423. 1.50 dollars. Water-Supply Paper 1392: Surface Water Supply of the United States, 1955. Part 8: Western Gulf of Mexico Basins. Prepared under the direction of J. V. B. Wells. Pp. x+443. 1.50 dollars. Water-Supply Paper 1393: Surface Water Supply of the United States, 1955. Part 9: Colorado River Basin. Prepared under the direction of J. V. B. Wells. Pp. xi+492. 1.75 dollars. Water-Supply Paper 1407: Water Levels and Artesian Pressures in Observation Wells in the United States, 1955. Part 4: South-Central States. Prepared under the direction of A. N. Sayre. Pp. vi+216. 75 cents. Water-Supply Paper 1408: Water Levels and Artesian Pressures in Observation Wells in the United States, 1955. Part 5: Northwestern States. Prepared under the direction of A. N. Sayre. Pp. vi+165. 60 cents. Water-Supply Paper 1411: The Deep Channel and Alluvial Deposits of the Ohio Valley in Kentucky. By Eugene H. Walker. Pp. iii+25+6 plates. n.p. (Washington, D.C.: Government Printing Office, 1957.) [269

United States Department of the Interior: Geological Survey Bulletin 1021–L: Geology of the Area East and Southeast of Livingston, Park County, Montana. By Paul W. Richards. Pp. iv+385–438+plates 34–35. 2.50 dollars. Bulletin 1040: Base-Metal Deposits of the Cordillera Negra, Departamento de Ancash, Peru. By Alfred J. Bodenlos and John A. Straczek. Pp. vi+165+14 plates. n.p. Bulletin 1045–B: Core Logs from Two Test Holes near Kramer, San Bernardino County, California. By D. D. Dickey. Pp. iii+63–80+plate 2. 45 cents. Bulletin 1059–A: Selected Annotated Bibliography of the Geology of Uranium-bearing Coal and Carbonaceous Shale in the United States. By Thomas M. Kehn. Pp. iii+28. 25 cents. Bulletin 1000-F: Principles of Geochemical Prospecting. By H. E. Hawkes. Pp. iv+225–356. 40 cents. Bulletin 1000-G: Geochemical Prospecting Abstracts, July 1952–December 1954. Pp. iii+357–395. 20 cents. Bulletin 1032-G: Geology of the Wood and East Calhoun Mines, Central City District, Gilpin County, Colorado. By Avery A. Drake, Jr. Pp. iv+129–170+plates 12–15. 1 dollar. Bulletin 1034: Mineral Deposits of Central America. By Ralph J. Roberts and Earl M. Irving. With a section on Manganese Deposits of Panama by Frank S. Simons. Pp. x+205+16 plates. n.p. Bulletin 1036–L: A Field Chromatographic Method for Determination of Uranium in Soils and Rocks. By Charles E. Thompson and H. W. Lakin. Pp. iii+209–220. 15 cents. Bulletin 1049: Bibliography of North American Geology, 1940–1949. By Ruth Reece King, Emma M. Thom, Elisabeth S. Loud and Marjorie Hooker. Part 1: Bibliography. Pp. iii+1034. Part 2: Index. Pp. iii+1035–2205. n.p. Bulletin 1059–B: Selected Annotated Bibliography of the Geology of Uranium-bearing Phosphorites in the United States. By Diane Curtis. Pp. iii+29–58. 20 cents. Bulletin 1066–A: Geophysical Abstracts, No. 168, January–March, 1957. By Mary C. Rabbitt, Dorothy B. Vitaliano, S. T. Vesselowsky, and others. Pp. iii+94. 25 cents. (Washington, D.C.: Government Printing Office, 1957.) [269

United States Department of the Interior: Geological Survey. Professional Paper 274-M: Metamorphism and the Origin of Granitic Rocks, Northgate District, Colorado. By T. A. Steven. Pp. iii+335–378+plates 48–55. n.p. Professional Paper 283: Mississippian Cephalopods of Northern and Eastern Alaska. By Mackenzie Gordon, Jr. Pp. iii+61+6 plates. 1.50 dollars. Professional Paper 290: Geology and Mineral Resources of the Congonhas District, Minas Gerais, Brazil. By Philip W. Guild. Pp. v+90+9 plates. n.p. Professional Paper 294-A: North American Mesozoic Charophyta. By Raymond E. Peck. Pp. iii+44+8 plates. 1 dollar. (Washington, D.C.: Government Printing Office, 1957.) [269

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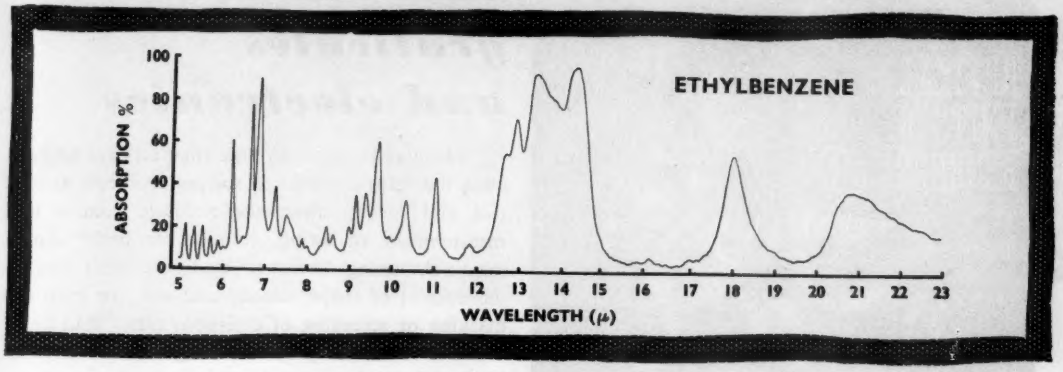

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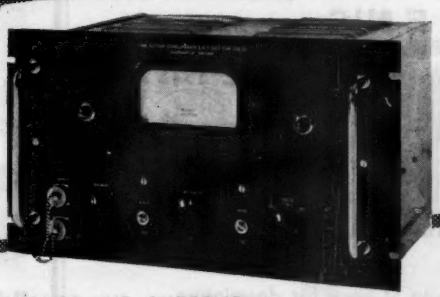

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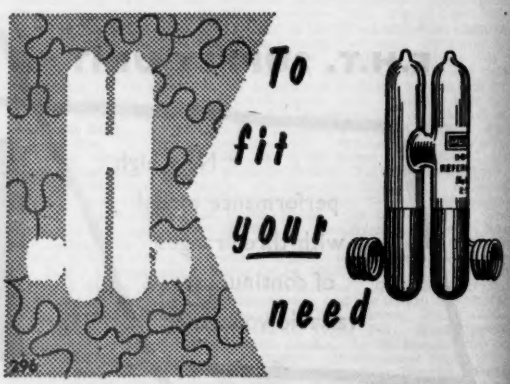

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